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ABSTRACT

This survey covers periodical literature published in the field of research on sexually transmitted diseases during 1985. The articles cover the following diseases: (1) genital chlamydial infection; (2) gonorrhea; (3) genital herpes infection; (4) human papillomavirus infection; (5) acquired immunodeficiency syndrome (AIDS); (6) genital cytomegalovirus infection; (7) syphilis; (8) pelvic inflammatory disease; (9) genital mycoplasma infection; (10) sexually transmitted diseases--general; (11) sexually transmitted diseases--other; (12) vaginitis; (13) sexually transmitted diseases--pregnancy; and (14) pharmacology. Article entries are organized by categories: clinical, laboratory diagnosis, and therapy. An informative abstract of the article is included and a selected bibliography accompanies each section. (JD)

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SURVEY OF RESEARCH ON SEXUALLY TRANSMITTED DISEASES

May 1987

U.S. DEPARTMENT OF HEALTH AND HUMAN SERVICES
PUBLIC HEALTH SERVICE
CENTERS FOR DISEASE CONTROL
CENTER FOR PREVENTION SERVICES
DIVISION OF SEXUALLY TRANSMITTED DISEASES
ATLANTA, GEORGIA 30333

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FOREWORD

Survey of Research on Sexually Transmitted Diseases covers periodical literature published in the field during 1985. Effort has been made to keep the abstracts in the survey sufficiently informative to enable the reader to decide whether the original article would be of interest to him or her. Bibliographies are also provided for reference purposes.

Publication of an abstract or a bibliographic reference does not imply endorsement by the United States Public Health Service of the original article or of any commercial products, drugs, or any other therapeutic modalities mentioned therein.

In compiling these bibliographies and abstracts, we utilized MEDLINE and SDILINE. MEDLINE is the National Library of Medicine's remote-access retrieval service. Under this system, 3,000 foreign and domestic biomedical periodicals are searched for material dealing with, or related to, sexually transmitted diseases. SDILINE (selective dissemination of information) lists, by month, the newest citations from journals indexed in NLM's *Index Medicus*. Other reference sources used in the preparation of this publication were the libraries of the Centers for Disease Control, Emory University, and other federal agencies.

Distribution of *Survey of Research on STD* is made to medical and other interested personnel and institutions throughout the United States and in 70 additional countries.

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Genital Chlamydial Infection

Clinical

Chlamydial Proctitis?

P.E. Munday, J.M. Carder and D. Taylor-Robinson. Genitourin Med 1985 Dec;61(6):376-8.

Chlamydia trachomatis was isolated from 21 (7%) of 309 specimens obtained in October 1982 from the rectum of homosexual men undergoing proctoscopy. During the same period, *Neisseria gonorrhoeae* was isolated from 12 (3%) of 454 specimens obtained similarly. The clinical features of patients infected with each of these micro-organisms were compared with those of an uninfected group of homosexual men. No characteristic diagnostic features were noted in the infected men.

Frequency of *Chlamydia trachomatis* as the Cause of Pharyngitis

H. Huss, D. Jungkind, P. Amadio and I. Rubenfeld. J Clin Microbiol 1985 Nov;22(5):858-60.

We evaluated the incidence of *Chlamydia trachomatis* as the etiologic agent of uncomplicated pharyngitis by the cell culture procedure recommended by the Centers for Disease Control, Atlanta, Ga., and by the MicroTrak direct immunofluorescent stain (Syva Co., Palo Alto, Calif.) for elementary bodies on throat swabs collected from 126 symptomatic patients. Of the 126 cultures, eight percent were positive for group A beta-hemolytic streptococci. Of 126 chlamydia cultures, none was positive. The MicroTrak test gave one borderline positive result. In contrast to a previously published report that *C. trachomatis* is the most frequent nonviral cause of adult pharyngitis (A. L. Komaroff, M. D. Aronson, T. M. Pass, C. T. Ervin, and W. T. Branch, Jr., Science 222:927-929, 1983), our data indicated an infection rate of less than one percent.

Chlamydial Infections of the Urethra in Women

M.G. Bradley, D. Hobson, N. Lee, I.A. Tait and E. Rees. Genitourin Med 1985 Dec;61(6):371-5.

Cervical and endourethral swabs from 360 untreated women attending a sexually transmitted disease (STD) clinic were cultured for *Chlamydia trachomatis* and other genitourinary pathogens. The patients included contacts of men with nongonococcal urethritis, women with gonorrhea, and those in whom symptoms suggestive of urinary tract infection were the main reasons for their attendance. Chlamydial infection of the urethra was less common than, and seldom occurred in the absence of, cervical chlamydial infection; it was frequently silent, producing no signs or symptoms of urethritis. Only 33/96 women with evidence of urethritis gave chlamydia positive urethral swabs, and 14 of them had other concurrent infections of the genitourinary tract. *Chlamydia trachomatis* thus does not appear to be a major cause of the signs and symptoms of urethritis commonly found in women attending STD clinics, and there seems to be no indication for taking routine urethral swabs to aid in the diagnosis of chlamydial infection in women.

Chlamydial Pneumonia in the Low Birthweight Neonate

A.A. Attenburrow and C.M. Barker. Arch Dis Child 1985 Dec;60(12):1169-72.

Low birthweight neonates who developed a severe pneumonia are described. *Chlamydia trachomatis* was isolated from the respiratory tract of all infants. They had protracted respiratory problems despite eradication of the organism by chemotherapy.

Efficacy of Maternal Screening and Therapy in the Prevention of Chlamydia Infection of the Newborn

J.A. McMillan, L.B. Weiner, H.V. Lamberson, J.H. Hagen, R.H. Aubry, R.W. Abdul-Karim, S.G. Sunderji and A.P. Higgins. Infection 1985 Nov-Dec;13(6):263-6.

Routine cervical cultures for chlamydia were obtained during the third trimester of pregnancy to identify infected mothers whose infants may also be infected. The effectiveness of maternal erythromycin therapy in preventing disease due to chlamydia among infants born to these women was also assessed. Clinical outcome of treated mothers and infants was compared to that of untreated subjects. Of 1,082 women who were cultured, 85 (7.8%) were positive for chlamydia. Erythromycin therapy was prescribed for 38 of these women. Nasopharyngeal/conjunctival chlamydia cultures were obtained from 16 infants of culture-positive, treated mothers and 21 infants of culture-positive, untreated mothers. None of the infants born to culture-positive, treated mothers developed infection with chlamydia, while five of 21 infants of untreated mothers (p less than 0.04) were culture-positive and symptomatic (four with conjunctivitis, one with pneumonia). On follow-up of the infants born to chlamydia-positive mothers, there was no evidence that chlamydia-infected infants had more frequent episodes of upper respiratory infection and otitis media during the first six months of life. This study demonstrated that diagnosis and treatment of cervical chlamydia infection during the third trimester of pregnancy provides a practical approach to the prevention of infection in the newborn.

The Microbiology of Nongonococcal Urethritis (NGU) in Singapore

K.B. Lim, C.T. Lee, T. Thirumoorthy, P.N. Arora, T. Tan and E.H. Sng. Ann Acad Med Singapore 1985 Oct;14(4):686-8.

Ninety-six men with nongonococcal urethritis (NGU) were studied to determine the microbiology of NGU in Singapore. *Chlamydia trachomatis* emerged as the most common etiologic agent, being isolated in 29 (30.2%) of 96 patients. The recovery rate of other potential pathogens and their significance locally are discussed.

Severe *Chlamydia psittaci* Sepsis in Pregnancy

A.W. McKinlay, N. White, D. Buxton, J.M. Inglis, F.W. Johnson, J.B. Kurtz and R.P. Brettle. Q J Med 1985 Oct;57(222):689-96.

Two patients with severe chlamydial sepsis in pregnancy are described and compared with previously published case reports. The infections appear to have been zoonotic, the patients acquiring their infections as a result of exposure to enzootic abortion of ewes. This is an important, but poorly recognized human infection which, because of its severity in pregnancy, deserves consideration in patients with an appropriate occupational history.

Chlamydia trachomatis: Its Role in Tubal Infertility

R.C. Brunham, I.W. Maclean, B. Binns and R.W. Peeling. J Infect Dis 1985 Dec;152(6):1275-82.

We compared the prevalence of antibody to *Chlamydia trachomatis* among 88 women undergoing an evaluation for infertility and 49 women attending an antenatal clinic. Demographic data regarding sexual behavior were also collected. Eighteen women had tubal infertility and 70 had infertility due to a variety of other reasons. In comparison with women who had other causes for infertility, women with tubal infertility began coitus sooner (17.7 +/− 2.2 years vs. 19.5 +/− 3.4 years, P less than .05) and had more lifetime sex partners (4.5 vs. 1.33, P less than .001). Women with tubal infertility had a higher prevalence of antibody to *C. trachomatis* (13 of 18) than did women with nontubal causes for infertility (6 of 70, P less than .0001) or pregnant women (11 of 49, P = .0003). This high prevalence of antibody to *C. trachomatis* among women with tubal infertility was independent of sexual experience. By immunoblot analysis, an antigen of approximately 57,000 Da was immunodominant in 11 of 13 seropositive subjects with tubal infertility vs. 2 of 6 seropositive subjects with nontubal infertility (P = .046) and 1 of 11 seropositive pregnant women (P = .0003). Thus, women with tubal infertility frequently have serological evidence of prior infection with *C. trachomatis* and have a distinctive antigen-specific humoral immune response. These results further support the etiologic role of infection with *C. trachomatis* in tubal infertility.

Failure of In Vitro Fertilization and Embryo Replacement Following Infection with *Chlamydia trachomatis*

G.F. Rowland, T. Forsey, T.R. Moss, P.C. Steptoe, J. Hewitt and S. Darougar. J In Vitro Fert Embryo Transfer 1985 Sep;2(3):151-5.

Antibodies to *Chlamydia trachomatis* were detected in 54 (47.4%) of 114 infertile women attending Bourn Hall Clinic. Antibodies were solely of the IgG class and mainly of a low titer, suggesting past infection. Antibodies were found in significantly more patients with tubal damage (54.4%) than in women whose infertility was due to other causes (16.6%). Seventy-two women completed in vitro fertilization, with 52 having three embryos replaced. We found that this treatment offered the optimum chance of a pregnancy being established, and 20 (38.5%) of these women became pregnant. Antibodies to *C. trachomatis* were present in only six (30.0%) of the women becoming pregnant, whereas antibodies were found in 21 (65.6%) of those who failed to become pregnant. Thus past infection with *C. trachomatis* halved the success rate of in vitro fertilization in these patients. The implications of these findings are relevant to all aspects of infertility from prevention to in vitro fertilization treatment.

Prevalence of *Chlamydia trachomatis* and Genital Mycoplasmas in Asymptomatic Women

J.A. Embil and L.H. Pereira. Can Med Assoc J 1985 Jul 1;133(1):34-5.

To establish the prevalence of *Chlamydia trachomatis*, *Mycoplasma hominis*, and *Ureaplasma urealyticum* in women attending a family planning and a prenatal clinic in Halifax, cervical swabs were obtained at the time of the first visit from 491 women who had no symptoms of genital infection. Among the women attending the family planning clinic, *M. hominis* occurred in combination with *C. trachomatis* more frequently than expected (p less than 0.05). It occurred in the absence of *U. urealyticum* in only a few cases (13% of the occurrences in the family planning clinic and 6% of those in the prenatal clinic). *C. trachomatis* was significantly more prevalent in women under 25

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years of age (p less than 0.04). However, mycoplasmas were as prevalent in women over 30 years as in those under 30. There were no significant differences in the infection rates of the organisms by trimester among pregnant women. More research is necessary for a proper understanding of the role of *M. hominis* and *U. urealyticum* in genitourinary infections and pregnancy outcomes.

Chlamydial Endometritis

J. Paavonen, R. Aine, K. Teisala, P.K. Heinonen, R. Punnonen, M. Lehtinen, A. Miettinen and P. Gronroos. J Clin Pathol 1985 Jul;38(7):726-32.

Endometrial biopsies were obtained from 32 women with suspected pelvic inflammatory disease, of whom 23 (72%) had histopathological evidence of endometritis. *Chlamydia trachomatis* was isolated from the endometria of nine (39%) women (chlamydia group) but not from the other 14 (non-chlamydia group). Severe plasma cell endometritis and lymphoid follicles with transformed lymphocytes were significantly more common in the chlamydia group than in the non-chlamydia group. This suggests that *C. trachomatis* is an invasive endometrial pathogen which often causes severe inflammation. The association was independent of predisposing factors such as use of intrauterine contraceptive devices.

Assessing the Number of Genital Chlamydial Infections in the United States

F.N. Judson. J Reprod Med 1985 Mar;30(3 Suppl):269-72.

The prevalence and incidence of genital infections with *Chlamydia trachomatis* have not yet been determined for broadly based populations within the United States. Largely on the basis of results of prevalence studies from sexually transmitted disease clinics, it has been estimated that *C. trachomatis* infections are the most common of all sexually transmitted infections and may number 3-5 million cases annually. *C. trachomatis* isolation rates range from 50 to 80 percent in certain diseases known to be caused by chlamydia, from 10 to 30 percent in sexually active female adolescents, and approximately 5 percent in college women. Cheaper, more sensitive, and widely available diagnostic tests are necessary to adequately define the epidemiology of genital chlamydia infections in the U.S.

Microbiology of Chronic Otitis Media with Effusion among Australian Aboriginal Children: Role of *Chlamydia trachomatis*

V.M. Dawson, R.J. Coelen, S. Murphy, D. Graham, H. Dyer and J. Sunderman. Aust J Exp Biol Med Sci 1985 Feb;63 (Pt 1):99-107.

Serum, eye secretions, post-nasal swabs, external ear swabs, and middle ear effusions (MEE) were collected from 131 Australian Aboriginal children with chronic otitis media with effusion (COME). The children were all resident in a trachoma endemic region. *Chlamydia trachomatis* was recovered from the MEE of two children. Probable bacterial pathogens were isolated from 34 (12.7%) ears. The remainder were sterile (52.4%) or contained normal skin flora (34.9%). Serum and secretions were examined by the microimmunofluorescent technique for the presence, titre and serotype of anti-chlamydial antibody. Antibody, predominantly of the C serotype, was found in a high percentage of sera (80%) and secretions (approximately 50%). This serotype is associated with ocular trachoma. It is concluded that *C. trachomatis* is associated with COME among some Aboriginal children in this trachoma endemic area.

The Clinical Presentation of *Chlamydia trachomatis* in a Urological Practice

J.B. Grant, P.J. Brooman, S.D. Chowdhury, P. Sequeira and N.J. Blacklock. Br J Urol 1985 Apr;57(2):218-21.

Fifty-nine men with *Chlamydia trachomatis* (CT) infection have been studied. Epididymitis was the most common presentation (26) compared with urethritis (8) and prostatitis (9). Only 13 patients gave a history of a urethral discharge. Fifteen of 21 female consorts screened were CT positive and 13 of these were asymptomatic. This demonstrates the major etiological role of CT in lower genitourinary infection and indicates the importance of screening and treating consorts.

Genital Infections with *Chlamydia trachomatis* in Women Attending an Antenatal Clinic

P.L. Wood, D. Hobson and E. Rees. Br J Obstet Gynaecol 1984 Dec;91(12):1171-6.

Cervical swabs for isolation of *C. trachomatis* and serum for anti-chlamydial antibodies were taken from 252 pregnant women on their first visit to an urban antenatal clinic. Chlamydial infection was found in 18 (7%) women, and antibody at titres greater than 1/32 in 48 (19%); of the 18 infected women only 10 (56%) showed antibody. The likelihood of infection could not have been predicted by urogenital symptoms, the social or medical history or serology. Hypertrophic cervical ectopy and mucopus were significantly more common in infected than in uninfected women but underestimate the true rate of infection. The consorts of 10 infected women had signs of nongonococcal urethritis but were asymptomatic; *C. trachomatis* was isolated from the urethra of one man. The indications for routine screening of antenatal patients for chlamydial infections is discussed.

Laboratory Diagnosis

Conventional Tissue Culture Compared with Rapid Immunofluorescence for Identifying *Chlamydia trachomatis* in Specimens from Patients Attending a Genitourinary Clinic

E.L. Teare, C. Sexton, F. Lim, T. McManus, A.H. Cutley and J. Hodgson. Genitourin Med 1985 Dec;61(6):379-82.

Specimens collected from 182 patients with histories suggesting chlamydial disease were examined by conventional culture and direct immunofluorescence techniques. *Chlamydia trachomatis* was identified by both methods in 57 percent of all patients. There was no significant difference between the two methods in detecting *C. trachomatis*. Where a tissue culture service is not already established, cost analysis in individual departments may justify the use of the immunofluorescence method.

Identification of *Chlamydia trachomatis* by Direct Immunofluorescence Applied in Specimens Originating in Remote Areas

T. Williams, A.C. Maniar, R.C. Brunham and G.W. Hammond. J Clin Microbiol 1985 Dec;22(6):1053-4.

The efficacy of the MicroTrak (Syva Co., Palo Alto, Calif.) direct immunofluorescence test for the detection of *Chlamydia trachomatis* was compared with cell culturing of fresh specimens obtained from patients attending a clinic on sexually transmitted disease and of frozen specimens delayed in transit from urban or remote physicians' offices and clinics. Direct immunofluorescence testing detected *C. trachomatis* more frequently than culturing of the same specimens when transit caused a delay in culturing.

Cervical Chlamydial Infections: Diagnostic Accuracy of the Papanicolaou Smear

R.B. Clark, V. Schneider, F.G. Gentile, B. Pechan and H.P. Dalton. South Med J 1985 Nov;78(11):1301-3.

To assess the reliability and accuracy of the Papanicolaou smear for the detection of cervical *Chlamydia trachomatis* infections, we obtained chlamydial cultures and cervical smears from 252 patients attending a gynecologic service during an eight-month time period. In 12 of these patients (4.8%), the cervical culture was positive for chlamydiae but the cytologic smear was negative for chlamydial inclusions. Five smears (2.2%) were cytologically positive for chlamydiae but were negative by culture. In none of the patients were both culture and smear positive for chlamydiae. In our experience, the smear was a completely unreliable test for the diagnosis of cervical *C. trachomatis* infections. The cytologic smear should not replace culture for the detection of chlamydial infections.

Detection of *Chlamydia trachomatis* Infection in Endocervical Specimens Using Direct Immunofluorescence

C.D. Graber, O. Williamson, J. Pike and J. Valicenti. Obstet Gynecol 1985 Nov;66(5):727-30.

A monoclonal antibody specific for *Chlamydia trachomatis* (Syva MicroTrak) was used to stain endocervical smears from three groups of women. When compared with results from tissue culture, direct specimen results showed 100 percent (15 of 15) sensitivity and 95 percent (164 of 172) specificity. The eight specimens with MicroTrak-positive/culture-negative results were probably true positives. Because the direct specimen test method takes less than an hour to complete, is easy to read with a fluorescence microscope, and is much less expensive than culture methods, it could become the rapid screening tool that is urgently needed in young, sexually active women.

Enzyme Amplified Immunoassay: A Novel Technique Applied to Direct Detection of *Chlamydia trachomatis* in Clinical Specimens

S.F. Pugh, R.C. Slack, E.O. Caul, I.D. Paul, P.N. Appleton and S. Gatley. J Clin Pathol 1985 Oct;38(10):1139-41.

Endocervical swabs from 212 women and urethral swabs from 100 men were tested by the routine methods for McCoy cell culture and simultaneously by a novel enzyme amplified immunoassay test to detect chlamydia antigen. Overall correlation of the amplified test with culture was 96.5 percent. The test proved to be a suitable screening procedure for genital chlamydial infection, particularly for large numbers of specimens or in cases in which culture was not available.

Effect of Swab Type and Storage Temperature on the Isolation of *Chlamydia trachomatis* from Clinical Specimens

J.B. Mahony and M.A. Chernesky. J Clin Microbiol 1985 Nov;22(5):865-7.

We evaluated various swabs for the recovery of *Chlamydia trachomatis* and found that only 7 of 14 swabs tested resulted in a greater than 50 percent recovery of organisms. Storage of chlamydial specimens at 4 degrees C for more than 1 day resulted in a rapid loss of viability, whereas freezing of specimens at -70 degrees C resulted in only a marginal decrease in the isolation rate.

Chlamydia trachomatis Infection Monitoring with Cytomorphology, Direct Immunofluorescence and "In Vitro" Growth Method

M.R. Cardillo, D. Sollecito, I. Coghi and M. Midulla. Eur J Gynaecol Oncol 1985;6(3):192-9.

The increased occurrence of genital infections from *Chlamydia trachomatis* (Ct) suggested the need for a simple, rapid, sensitive method for detection of Ct. The purpose of the present study was to select symptomatic or asymptomatic women through two fast screenings: Pap-test and direct immunofluorescence (IF) test with monoclonal antibody. From 1,816 cervical cytology samples, 32 (1.76%) were selected for intracytoplasmic inclusions pathognomonic of Ct infection. Only 19 women underwent a check-up. The direct IF gave positive results in ten cases out of 19 (52.63%), and culture in eleven (57.89%). A correlation was made between the direct IF test and culture and also between cytologic and colposcipc findings. We thus conclude that direct IF, for its specificity, sensitivity, easy execution and low cost, could be currently utilized when clinical signs or Pap smears are suggestive of Ct infections.

Rapid, Reliable Diagnosis of Chlamydial Ophthalmia by Means of Monoclonal Antibodies

D.A. Hawkins, R.S. Wilson, B.J. Thomas and R.T. Evans. Br J Ophthalmol 1985 Sep;69(9):640-4.

The use of fluorescein-conjugated monoclonal antibody (Syva, UK) provided a rapid reliable diagnostic test for *Chlamydia trachomatis* in conjunctival samples from 100 adults with acute follicular conjunctivitis and seven babies with suspected chlamydial ophthalmia neonatorum. Elementary bodies (EBs) were seen in smears from 11 of the adults, and culture confirmed *C. trachomatis* infection in nine of them. Both tests were positive with specimens from four of the neonates. No specimens from either group of patients produced a negative result in the smear test but a positive result by culture. However, the two adult patients with chlamydial ophthalmia who had negative cultures but were EB-positive had both had prior topical tetracycline therapy.

The Cytologic Features of Chlamydial Cervicitis

L.E. Lindner, S. Geerling, J.A. Nettum, S.L. Miller and K.H. Altman. Acta Cytol (Baltimore) 1985 Sep-Oct; 29(5):676-82.

Chlamydial cervicitis is a common and important infection. Diagnostic cytologic criteria have been proposed, but not generally accepted. To better evaluate the cytologic changes, cervical cultures for *Chlamydia trachomatis* and duplicate cervical smears for Papanicolaou staining and immunofluorescence staining for chlamydial organisms were taken from 496 patients. A total of 61 (12.3%) of the patients had a positive culture for *C. trachomatis.* By immunofluorescence, the organisms were present as very small extracellular elementary bodies in mucus or as similar bodies in leukocytes; inclusions within epithelial cells were seen in only two cases. The organisms did not stain with the Papanicolaou stain. Chlamydial infection correlated with the degree of inflammation, with the presence of histiocytes and lymphocytes, especially large "transformed" lymphocytes, and with the presence of unidentified short bacteria, which stained red with the Papanicolaou stain. These features predict which patients should be tested more definitively for the presence of chlamydial organisms. However, we found no cytologic criteria that can reliably permit its diagnosis.

Sensitivity and Specificity of the Papanicolaou-Stained Cervical Smear in the Diagnosis of *Chlamydia trachomatis* Infection

S. Geerling, J.A. Nettum, L.E. Lindner, S.L. Miller, L. Dutton and S. Wechter. Acta Cytol (Baltimore) 1985 Sep-Oct;29(5):671-5.

Two hundred young women had simultaneously prepared cultures for *Chlamydia trachomatis* and cervical smears; they also completed a questionnaire. Twelve of the chlamydial cultures were positive. There was poor correlation between the culture results and the cytologic morphology or symptoms. On initial blind reading, only 10 percent of the smears cytologically interpreted as positive were actually positive by culture. Under the most favorable (non-blind) interpretation, only 23 percent of the smears cytologically interpreted as positive for chlamydial infection were also culture positive. Because of the high incidence of false positives, we conclude that routine cytologic examination of Papanicolaou-stained smears is not an acceptable method for the diagnosis of chlamydial infections of the cervix. Immunoperoxidase staining of duplicate smears did not appear to be a successful replacement for culture.

Is One Swab Enough to Detect Chlamydial Infection of the Cervix?

P.E. Munday, J.M. Carder, N.F. Hanna and D. Taylor-Robinson. Br J Vener Dis 1984 Dec;60(6):384-6.

Three swabs were taken from the cervix of each of 104 women for the detection of *Chlamydia trachomatis.* The processing of three swabs instead of one increased the isolation rate by only 2 percent, and later swabs did not result in the production of more chlamydial inclusions than first swabs. In most clinics, therefore, a single cervical swab is adequate to detect chlamydial infection.

Triple-Culture Tests for Diagnosis of Chlamydial Infection of the Female Genital Tract

E.M. Dunlop, B.T. Goh, S. Darougar and R. Woodland. Sex Transm Dis 1985 Apr-Jun;12(2):68-71.

By use of triple-culture tests of each site, *Chlamydia trachomatis* was isolated from 112 women: from cervical material from 110, urethral material from 32, and rectal material from 19. Triple swabs provided 89 (81%) of 110 diagnoses of cervical infection; the first swab yielded 65 (59%), the second an additional 15 (14%), and the third an additional nine (8%). Three sets of cervical scrapings provided 102 (93%) of 110 diagnoses of cervical infections; the first scrapings yielded 76 (69%), the second an additional 22 (20%), and the third another four (4%). Of 32 women with positive urethral cultures, the first swab was positive in 28 (88%), and the second in the remaining four. Of 19 women with positive rectal cultures, the first swab yielded 11 (58%), the second an additional five (26%), and the third an additional three (16%). The results show that positive culture results obtained by use of a single swab underestimate the prevalence of chlamydial infection.

Chlamydia trachomatis in the Pharynx and Rectum of Heterosexual Patients at Risk for Genital Infection

R.B. Jones, R.A. Rabinovitch, B.P. Katz, B.E. Batteiger, T.S. Quinn, P. Terho and M.A. Lapworth. Ann Intern Med 1985 Jun;102(6):757-62.

Although urogenital infections with *Chlamydia trachomatis* are well recognized, less is known about infection at other body sites in adults. Pharyngeal specimens obtained from 706 heterosexual men and 686 women, and rectal specimens obtained from 1,223 women who were at risk for chlamydia infection were cultured for *C. trachomatis*. Urogenital specimens were obtained from all patients. *Chlamydia trachomatis* was isolated from the pharynx in 3.7 percent of men and 3.2 percent of women. Recovery of chlamydiae was not associated with the presence of pharyngeal symptoms, but in women, but not men, it was associated with a history of oral-genital sex. The organism was also recovered from the rectum of 5.2 percent of the women. Rectal isolation did not correlate with a history of rectal symptoms or rectal sex but did correlate with concurrent genital infection. Infection at these sites may be important in the transmission or persistence of *C. trachomatis* infections.

Detection of *Chlamydia trachomatis* in Clinical Specimens by Nucleic Acid Spot Hybridization

T. Hyypia, A. Jalava, S.H. Larsen, P. Terho and V. Hukkanen. J Gen Microbiol 1985 Apr;131 (Pt 4):975-8.

A nucleic acid spot hybridization assay was used to detect *Chlamydia trachomatis* DNA. The hybridization probes included DNA isolated from elementary bodies of lymphogranuloma venereum (LGV) strains and cloned fragments of both chromosomal and plasmid DNA. The sensitivity of the test was in the range 10 to 100 pg homologous DNA and 10 in vitro infected cells. Cross-reactivity with bacterial DNA was avoided when purified chlamydia-specific DNA fragments were used as probes. *C. trachomatis* was detectable in most of the clinical specimens with large amounts of infectious particles. Also some isolation-negative specimens gave a positive signal in the test.

Comparison of Enzyme Linked Immunosorbent Assay and Enzyme Linked Fluorescence Immunoassay for Detection of Antibodies against *Chlamydia trachomatis*

K. Numazaki, S. Chiba, T. Moroboshi, T. Kudoh, T. Yamanaka and T. Nakao. J Clin Pathol 1985 Mar;38(3):345-50.

An enzyme linked fluorescence immunoassay (ELFA) has been evaluated for the detection of antibodies against *Chlamydia trachomatis*. Reticulate bodies and elementary bodies from *C. trachomatis* L2/434 strain were used as antigens. An enzyme linked immunosorbent assay (ELISA) has also been evaluated using the same antigens. Results obtained by ELISA and ELFA for human sera with these two antigens were compared with each other and with the results obtained by a micro-immunofluorescence (micro-IF) test. Serum IgG antibodies against *C. trachomatis* L2 reticulate bodies and elementary bodies were found in 32 (20.0%) and 11 (6.9%), respectively, of 160 serum samples from pregnant women by the micro-IF test (titre greater than or equal to 1/32). All of these 32 pregnant women had IgG antibodies to *C. trachomatis* reticulate bodies (titre greater than or equal to 1/100), whereas 20 (12.5%) had IgG antibodies to elementary bodies in the ELISA. On the other hand, 25 (15.6%) and 19 (11.9%) of them had IgG antibodies to *C. trachomatis* L2 reticulate bodies and elementary bodies, respectively, by the ELFA (titre greater than or equal to 1/500).

Enzyme Immunoassay for Detection of *Chlamydia trachomatis* from the Cervix

A.J. Amortegui and M.P. Meyer. Obstet Gynecol 1985 Apr;65(4):523-6.

An enzyme immunoassay for the detection of *Chlamydia trachomatis* antigens was compared with isolation of the organism in cycloheximide-treated McCoy cells using duplicate cervical swab specimens from 514 women. *Chlamydia trachomatis* was isolated after subculturing from 45 of 514 (8.8%) specimens, while the enzyme immunoassay, Chlamydiazyme detected chlamydial antigens in 37 of 45 (82.2%) of those women. Chlamydiazyme was as sensitive as primary isolation for detecting total infections. The specificity of Chlamydiazyme was 98.1 percent. The predictive values of a positive and negative Chlamydiazyme test compared with isolation after subculturing was 80.4 and 98.3 percent, respectively. Overall, 497 of 514 (96.7%) samples were identified correctly by Chlamydiazyme. Thus, Chlamydiazyme is a simple and rapid test that eliminates many of the problems encountered by isolation procedures.

Cytologic Manifestations of Cervical and Vaginal Infections. II. Confirmation of *Chlamydia trachomatis* Infection by Direct Immunofluorescence Using Monoclonal Antibodies

N.B. Kiviat, M. Peterson, E. Kinney-Thomas, M. Tam, W.E. Stamm and K.K. Holmes. JAMA 1985 Feb 15;253(7):997-1000.

We found inflammatory patterns of transparent lymphocytes on increased numbers of histiocytes suggestive of chlamydial infection in 68 (56%) of 121 cervical cytologic smears. *Chlamydia trachomatis* was isolated from 36 (53%) of those with and only two (4%) of those without such inflammatory patterns. Direct stain with fluorescein-conjugated monoclonal antibodies demonstrated elementary bodies of *C. trachomatis* in 30 (79%) of the 38 culture-positive patients, including 29 of the culture-positive patients who had an inflammatory cytologic pattern suggestive of *C. trachomatis* infection. Thus, Papanicolaou smears can be screened for inflammatory pattern, and separate endocervical smears from patients with a pattern suggestive of chlamydial infection can then be stained by immunofluorescence to confirm the presence of *C. trachomatis* infection. This two-step approach detected 29 of 38 infections confirmed by culture in the present study, giving a sensitivity of 76 percent, a specificity of 100 percent, and a positive predictive value of 100 percent in a population having a 31 percent prevalence of *C. trachomatis* infection.

Cytologic Manifestations of Cervical and Vaginal Infections. I. Epithelial and Inflammatory Cellular Changes

N.B. Kiviat, J.A. Paavonen, J. Brockway, C.W. Critchlow, R.C. Brunham, C.E. Stevens, W.E. Stamm, C.C. Kuo, T. DeRouen, and K.K. Holmes. JAMA 1985 Feb 15;253(7):989-96.

We used multiple logistic regression to analyze microbiological and clinical correlates of inflammatory and epithelial cell changes on Papanicolaou-stained cervical smears in patients from a sexually transmitted disease clinic. Among randomly selected patients, increased numbers of histiocytes and polymorphonuclear leukocytes and the presence of transformed lymphocytes were associated with *Chlamydia trachomatis* infection, while increased lymphocytes were associated with *Trichomonas vaginalis* infection; minimal squamous atypia was associated with yeast infection; and moderate squamous atypia and koilocytosis were associated with cervical condylomata visualized by colposcopy. Among patients referred for cervicitis, *C. trachomatis* infection was also associated with reactive or atypical metaplastic cells. Distinct inclusions were seen by Papanicolaou smear in only 22 percent of *C. trachomatis* infections. In randomly selected patients, however, the presence of transformed lymphocytes or increased histiocytes had a sensitivity of 95 percent, a specificity of 75 percent, and a positive predictive value of 50 percent in relation to isolation of *C. trachomatis*, and could therefore be used for selection of patients for confirmatory testing for *C. trachomatis* infection.

Therapy

Experience with the Routine use of Erythromycin for Chlamydial Infections in Pregnancy

J. Schachter, R.L. Sweet, M. Grossman, D. Landers, M. Robbie and E. Bishop. N Engl J Med 1986 Jan 30;314(5):276-9.

In an effort to prevent perinatal acquisition of *Chlamydia trachomatis*, we offered treatment with erythromycin ethylsuccinate (400 mg four times a day for seven days, given at 36 weeks' gestation) to 184 pregnant women with cervical chlamydial infections. Thirty-two women refused treatment; 24 of their infants were followed and served as the controls. Therapy was discontinued by 5 of 10 women who had gastrointestinal disturbances. Forty-seven women who completed therapy refused infant follow-up; in four (9%) of these women, therapy had failed to eradicate the infection. Sixty women and 59 infants completed the entire protocol; 55 (92%) of the women had negative cultures for chlamydia at follow-up. Chlamydial infection developed in 4 (7%) of the 59 infants of treated mothers, as compared with 12 (50%) of the 24 infants of untreated mothers; this difference was significant (P less than 0.001). With a success rate of 92 percent (98 of 107 patients) in treating maternal infection and with a relatively low intolerance rate (3%; 5 of 152), this regimen appears to be an effective, although not ideal, therapy for chlamydial infection in pregnant women. We conclude that in settings in which the prevalence of chlamydia infection is high, a routine program of screening pregnant women for cervical *C. trachomatis*, followed by treatment of those infected, would be cost effective and would reduce infant morbidity.

Activity of Thiamphenicol Against *Chlamydia trachomatis* and *Neisseria gonorrhoeae*

G.L. Ridgway, D. Felmingham, G. Mumtaz and M. O'Hare. Sex Transm Dis 1984 Oct-Dec;11(4 Suppl): 432-4

The in vitro activity of thiamphenicol against *Neisseria gonorrhoeae* was compared with that of penicillin. A total of 267 isolates were tested. All strains were inhibited by less than or equal to 4.0 micrograms of thiamphenicol/ml. However, the minimal inhibitory concentration of thiamphenicol was fourfold higher (MIC90 = 2.0 micrograms/ml) for beta-lactamase-producing strains or those moderately resistant to penicillin than for penicillin-sensitive strains (MIC90 = 0.5 micrograms/ml). The MIC of thiamphenicol for *Chlamydia trachomatis* was determined for a control strain and for 15 recent clinical isolates. The MIC90 for thiamphenicol was 1.0 micrograms/ml, as compared with a MIC90 of oxytetracycline of 0.12 micrograms/ml against the same isolates.

In Vitro Activity of the Spermicide Nonoxynol-9 against *Chlamydia trachomatis*

J.P. Kelly, R.B. Reynolds, S. Stagno, W.C. Louv and W.J. Alexander. Antimicrob Agents Chemother 1985 May;27(5):760-2.

The in vitro activity of nonoxynol-9 against four serotypes (C, D, H, and K) of *Chlamydia trachomatis* was investigated. A constant inoculum of each serotype was exposed to serial twofold dilutions (1:100 to 1:800) of Koromex, Conceptrol, or reference preparations (not containing nonoxynol-9) for 4 and 24 hours at 37 degrees C. The mixtures of nonoxynal-9 or nonnonoxynol preparations and control inocula were dispensed into triplicate wells containing McCoy cell monolayers. After incubation at 37 degrees C, the monolayers were fixed and stained with iodine and examined for evidence of infection with *C. trachomatis.* All nonoxynol-9-containing preparations showed marked antichlamydial activity as judged by percent reduction of glycogen-containing intracytoplasmic inclusions. The reference preparations, which did not contain nonoxynol-9, were markedly less active when tested in this in vitro system.

Inhibition of Growth of *Chlamydia trachomatis* by Nonoxynol-9 In Vitro

S. Benes and W.M. McCormack. Antimicrob Agents Chemother 1985 May;27(5):724-6.

We evaluated the ability of the widely used spermicide nonoxynol-9, Conceptrol gel containing nonoxynol-9, and Conceptrol vehicle (without nonoxynol-9) to inhibit the formation of inclusions of *Chlamydia trachomatis* in cycloheximide-treated McCoy cells. Conceptrol vehicle produced a non-dose-related 40 to 59 percent reduction of the number of inclusions formed. In contrast, the addition of nonoxynol-9 and Conceptrol gel containing nonoxynol-9 at a concentration of 100 micrograms/ml reduced the number of inclusions by 84 to 95 percent. Prolongation of contact between nonoxynol-9 and the chlamydial organisms from 90 to 180 minutes did not result in additional inhibition. Using a higher concentration of chlamydial organisms and diluting the drug-chlamydia mixture before inoculation of the monolayers, we were able to test higher concentrations of nonoxynol-9. At concentrations of 100 to 5,000 micrograms of nonoxynol-9 per ml, a dose-related 19 to 84 percent reduction of the number of inclusions was noted.

Topical Sulfacetamide vs. Oral Erythromycin for Neonatal Chlamydial Conjunctivitis

A.D. Heggie, A.C. Jaffe, L.A. Stuart, P.S. Thombre and R.U. Sorensen. Am J Dis Child 1985 Jun;139(6):564-6.

Conjunctival and nasopharyngeal cultures for *Chlamydia trachomatis* were obtained from infants 30 days of age or younger with purulent conjunctivitis. Conjunctival specimens were also tested for other bacterial pathogens and for viruses. Most of the infants studied were black and came from a low-income, urban population. By random assignment, infants received either topical treatment with 10 percent sulfacetamide sodium ophthalmic solution or systemic treatment with oral erythromycin estolate (50 mg/kg/day). Treatment was continued for 14 days if *C. trachomatis* was isolated from the conjunctivae. Treatment was considered to be effective if conjunctivitis resolved and if follow-up chlamydial cultures of the conjunctivae and nasopharynx were negative at completion of therapy and two to four weeks later. *Chlamydia trachomatis* was isolated in the absence of other pathogens from the eyes of 37 (73%) of 51 infants with conjunctivitis. Other bacterial pathogens were isolated from four infants (8%) and viruses from none. Chlamydial infection was eradicated from 14 (93%) of 15 infants treated orally. In contrast, persistent conjunctival infection was detected in eight infants (57%) and nasopharyngeal colonization in three (21%) of 14 infants after topical treatment. It was concluded that *C. trachomatis* is the most frequent cause of neonatal conjunctivitis in the low-income, urban population studied; that erythromycin estolate administered orally for 14 days eradicates chlamydial conjunctival and nasopharyngeal infection; and that topical sulfacetamide therapy may result in persistent conjunctival infection and nasopharyngeal colonization.

Erythromycin Stearate in Treating Chlamydial Infection of the Cervix

J.M. Hunter and R.G. Sommerville. Br J Vener Dis 1984 Dec;60(6):387-9.

A total of 157 women attending departments of genitourinary medicine were treated for chlamydial infection of the cervix with erythromycin stearate 500 mg twice a day. Chlamydiae were eradicated from the cervix in 64/80 women treated for seven days and in 51/77 women treated for 14 days. In 12 of those treated for seven days and 15 of those treated for 14 days, reinfection was the probable cause of reisolation after treatment. The possibility of latent infection with *Chlamydia trachomatis* could not be excluded in five women, but was not more likely to occur with the shorter treatment course. Erythromycin stearate 500 mg twice daily for seven days appears to be an effective regimen for the treatment of uncomplicated chlamydial infection of the cervix.

Research and Evaluation

Overview of *Chlamydia trachomatis* Infection and the Requirements for a Vaccine

J. Schachter. Rev Infect Dis 1985 Nov-Dec;7(6):713-6.

Chlamydia trachomatis is an important human pathogen. The development of vaccines designed to prevent *C. trachomatis*-associated morbidity would be highly desirable. In the developing world, the major goal is the prevention of blindness due to trachoma; in industrialized societies and in some developing countries, the major goal is the prevention of chlamydial salpingitis and its consequences. In early trials of trachoma vaccine composed of a suspension of elementary bodies (the infectious particles), short-lived protective immunity was induced, but deleterious effects, i.e., hyperreactivity to infection, were also noted. Thus it is likely that separation of the protective from the sensitizing antigens and the development of a subunit vaccine will be necessary. Chlamydial virulence factors include the surface structures (presumably antigenic) that are responsible for specific attachment of the organism to a susceptible host cell, induction of phagocytosis by the host cell, or inhibition of phagolysosomal fusion. Serotype-specific neutralizing antigens might also be candidate antigens. Purification of such subunit antigens from chlamydial particles is probably impractical. It is likely that genetic engineering will be required for the production of cloned antigens after such antigens have been identified.

Chlamydial Pneumonitis Induced in Newborn Guinea Pigs

R.G. Rank, A.J. Hough, Jr., R.F. Jacobs, C. Cohen and A.L. Barron. Infect Immun 1985 Apr;48(1):153-8.

One- to three-day-old guinea pigs were inoculated intranasally with the chlamydial agent of guinea pig inclusion conjunctivitis. Physical signs of infection included a marked increase in respiration rate on days 5 to 10 of infection and radiographic evidence of pneumonia on day 6. When animals were killed at various times after infection and lung tissue was examined by histopathology, evidence of pneumonia was found beginning on day 4 and lasting as long as day 12, with maximal pathological changes on days 6 to 8. The pneumonia was generally unilateral and consisted of an acute inflammatory component in the bronchioles with granulocytes in both the lumen and the wall of the bronchioles and an interstitial and intra-alveolar mononuclear infiltrate in the parenchyma of the lung. Chlamydial antigen was detected in the bronchial epithelial cells by immunoperoxidase staining, and the guinea pig inclusion conjunctivitis organism was isolated from lung tissue on days 6 to 9. No other significant bacteria were isolated from lung tissue or seen on gram stains of lung sections. Both immunoglobulin M and immunoglobulin G serum antibodies to the guinea pig inclusion conjunctivitis agent were detected as early as day 8 and reached peak levels on day 12. The infection was apparently self-limiting. This model presents the opportunity to investigate pathophysiological and immunological aspects of chlamydial respiratory infections in a neonatal animal.

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Gonorrhea

Clinical

Chromosomally Mediated Resistance in *Neisseria gonorrhoeae* in the United States: Results of Surveillance and Reporting, 1983-1984

R.J. Rice, J.W. Biddle, Y.A. JeanLouis, W.E. DeWitt, J.H. Blount and S.A. Morse. J Infect Dis 1986 Feb;153(2):340-5.

Between January 1983 and October 1984, 446 cases of infection due to chromosomally mediated resistance in *Neisseria gonorrhoeae* (CMRNG) were reported in 23 states. Eighty percent were detected as primary penicillin or ampicillin treatment failures. Gonococcal isolates were submitted from 175 (40%) for confirmation of resistance, susceptibility testing, gonococcal strain typing using monoclonal antibodies specific for outer membrane Protein I, and auxotyping. All were typed as Protein I serogroup IB (WII/WIII), and the majority were proline or prototrophic auxotypes. All were resistant in vitro to less than 1 microgram/ml of either penicillin or tetracycline. Comparing CMRNG with penicillinase-producing *Neisseria gonorrhoeae* (PPNG), we found that CMRNG were significantly more resistant to tetracycline and erythromycin, but PPNG were more resistant to penicillin (P less than .01). Because of increasing reports of gonococcal resistance in the United States, improved surveillance of clinical and laboratory resistance is needed in support of control and treatment recommendations for gonorrhea.

Hemorrhagic *Neisseria gonorrhoeae* Conjunctivitis in an Adolescent Female

R.M. Buchta. J Adolesc Health Care 1986 Jan;7(1):60-1.

Gonococcal conjunctivitis in adults is rare; however, over the past two years there have been reports of cases from the military and an outbreak of ten cases in Miami, where urine was used as therapy for hemorrhagic conjunctivitis. Reported here is the case of a sixteen-year-old female who developed hemorrhagic conjunctivitis that grew *Neisseria gonorrhoeae*. With the increase in sexual activity at younger ages, gonococcal conjunctivitis may become more prevalent in this age group.

Serologic Classification and Contact-Tracing in the Control of Microepidemics of Beta-Lactamase-Producing *Neisseria gonorrhoeae*

K.M. Ramstedt, G.J. Hallhagen, S.M. Bygdeman, K.A. Lincoln, I. Kallings, C. Gillenius and E.G. Sandstrom. Sex Transm Dis 1985 Oct-Dec;12(4):209-14.

Serologic classification of isolated gonococcal strains and thorough contact-tracing were proved to be valuable in controlling an indigenous outbreak of infections caused by beta-lactamase-producing *Neisseria gonorrhoeae* (PPNG). Only 1-2 percent of gonococcal strains isolated in Sweden are PPNG, and before 1983 most of them were imported. During January-August 1983, 43 PPNG strains were isolated from 42 patients in Gothenburg. The PPNG strains were auxotyped and classified serologically. PPNG strains of serogroup WI, serovar (subgroup) Ae and of the prototrophic auxotype were isolated from 27 patients, including six prostitutes. Information obtained at interviews with these patients indicated that there had been a chain of infections. Quick and thorough contact-tracing stopped this microepidemic within three months. The serologic classification of the PPNG strains helped us to concentrate the epidemiologic efforts on those persons known to be infected with the epidemic strain, to trace this infection to other parts of Sweden, and to determine when the outbreak was finished.

Predictors of Asymptomatic Gonorrhea among Patients Seen by Private Practitioners

R. Allard, J. Robert, P. Turgeon and Y. Lepage. Can Med Assoc J 1985 Dec 1;133(11):1135-9, 1146.

Nineteen physicians participating in a program for detecting and treating gonorrhea and other sexually transmitted diseases (STD) in high-risk groups filled out encounter forms for the initial visits by the first 3,144 patients. This information was used to describe the program users and, by means of logistic regression analysis, to identify predictors of gonorrhea in asymptomatic patients. Overall, 17.3 percent of the users had culture-proved gonorrhea. Of the symptomatic patients, 24.5 percent had gonorrhea. Of the asymptomatic patients, 20.4 percent of those with a history of contact with a known or suspected case of STD had the disease, and 5.3 percent of those without a history of contact had the disease. The independent predictors of gonorrhea identified were, in order of importance, a history of contact with a case of STD and being less than 30 years of age. These predictors underline the importance of contact tracing, an underused but productive method of gonorrhea control that can be used effectively in private practice.

A Civilian-Military Partnership to Reduce the Incidence of Gonorrhea

D.E. Woodhouse, J.J. Potterat, J.B. Muth, C.I. Pratts, R.B. Rothenberg and J.S. Fogle, II. Public Health Rep 1985 Jan-Feb;100(1):61-5

To reduce the incidence of gonorrhea in the Colorado Springs, Colorado area, casefinding measures (interviewing of patients and tracing of contacts) were conscientiously applied by the local health department, in cooperation with the U.S. Army, to more than 90 percent of reported cases during a 3-year period. Nearly 4,000 cases of gonorrhea—2,127 civilian and 1,811 military—were interviewed; they named 7,399 contacts. A total of 1,141 cases of gonorrhea were newly identified and patients brought to treatment in Colorado Springs as a result. Implementation of these measures was associated with a 12.9 percent overall decline in gonorrhea incidence. This decline was most pronounced in the civilian population (20%), while little change in incidence occurred in the military population. The data presented suggest that the orderly application of casefinding epidemiology, allied with other control program initiatives, can interrupt transmission of, and prevent, disease.

Susceptibility to Antimicrobials of *Neisseria gonorrhoeae* Isolated in Singapore: Implications on the Need for More Effective Treatment Regimens and Control Strategies

E.H. Sng, A.L. Lim and K.L. Yeo. Br J Vener Dis 1984 Dec;60(6):374-9

The antimicrobial susceptibility of gonococci isolated in Singapore has been studied over several years. In 1983, the prevalence of penicillinase-producing *Neisseria gonorrhoeae* (PPNG) was 33.5 percent and 64 percent of non-PPNG isolates had minimum inhibitory concentrations (MICs) of penicillin of greater than or equal to 0.5 mg/l. After a control program, the isolation of the gonococcus from prostitutes was reduced and there was improvement in its susceptibility to antimicrobials. The incidence of PPNG strains was stabilized with a change in the treatment regimen. An influx of foreign prostitutes, however, had an unfavorable impact on these variables. Countries in South East Asia have a high prevalence of PPNG and non-PPNG strains that have reduced susceptibility to antimicrobials. In view of increased air travel, the problem should be seen from a global perspective. Better treatment regimens and control strategies are urgently needed.

Disseminated Gonococcal Infection in a Married Couple

R.H. Withrington and M.H. Seifert. Clin Rheumatol 1985 Jun;4(2):181-2.

The rare occurrence of disseminated gonococcal infection in a married couple is reported. These cases support the concept that bacterial rather than host factors are more important in determining the disease manifestations in gonorrhea.

A Community-Based Outbreak of Infection with Penicillin-Resistant *Neisseria gonorrhoeae* not Producing Penicillinase (Chromosomally Mediated Resistance)

H. Faruki, R.N. Kohmescher, W.P. McKinney and P.F. Sparling. N Engl J Med 1985 Sep 5;313(10):607-11.

From February through November of 1983, 199 cases of penicillin-resistant *Neisseria gonorrhoeae* infection were identified in a localized epidemic in Durham, North Carolina. The isolates did not produce beta-lactamase but were unusually resistant to penicillin (minimum inhibitory concentration, 2.0 to 4.0 micrograms per milliliter), and 15 of 16 patients treated with 4.8 million units of penicillin G procaine plus 1.0 g of probenecid did not respond to therapy. Recognition of the outbreak was impeded by a lack of routine surveillance for resistance other than that mediated by beta-lactamase. All epidemic isolates had a single serotype, auxotype, and antibiotic-susceptibility profile. The outbreak was halted by changing the treatment for all patients and their contacts to spectinomycin, and by intensive epidemiologic casefinding efforts. The emergence of such resistant strains poses potential major public health problems and indicates a need for reassessment of current surveillance procedures.

Increased Frequency of Carcinoma of the Uterine Cervix in Women Married to Men with a Previous Gonorrheal Infection. An Epidemiological Study

S. Furgyik. Acta Obstet Gynecol Scand 1985;64(3):245-9.

An earlier investigation showed an increased frequency of squamous epithelial carcinoma of the cervix in women who had experienced gonorrhea, but that there was a long lag between the infection and diagnosis of the cervical malignancy. The present work is a retrospective study of cervical malignancy in women married to men who had had gonorrhea between 26 and 37 years previously. The women have been distributed into three groups: i) those who were married to their spouse at the time he had gonorrhea and who themselves became infected, ii) those who were married to their spouse at the time of his gonorrhea but who did not themselves become infected, iii) those who were not married to the man in question at the time of his gonorrhea and who do not recall having had gonorrhea. The incidence rates of cervical neoplasm were found to be: group i, 27.1 percent, group ii, 21.7 percent, and group iii, 13.7 percent. For all three groups the figures are significantly higher than in an age-related control group drawn from the normal population. The results of the investigation lead one to suspect that a carcinogenic agent had been transferred by sexual intercourse together with the gonorrhea and that the man was the bearer of this agent long after he had undergone treatment for his gonorrhea, but that not all the women so exposed had developed a cervical neoplasm.

Gonorrhea as a Social Disease

J.J. Potterat, R.B. Rothenberg, D.E. Woodhouse, J.B. Muth, C.I. Pratts and J.S. Fogle, II. Sex Transm Dis 1985 Jan-Mar;12(1):25-32.

Gonococcal infection in Colorado Springs, Colorado, is concentrated in about 1 percent of the population. The social groups at risk are characterized as young, nonwhite, heterosexual, and connected to the military. They exhibit residential proximity by clustering in "core" census tracts; 51 percent of cases were in four tracts. They demonstrate residential stability and close social association at preferred sites for nighttime leisure activity (six major sites out of 300 available). Social aggregation is further demonstrated by the length of social contact prior to sexual contact (45% had known each other for over two months), the neighborhood nature of sexual choices, and the grouping of sexually connected individuals in lots (six lots contained 20% of cases). The force of infectivity, measured in person-days of potential spread of gonorrhea by infected contacts, provides a quantitative assessment of the importance of identifiable social groups in the transmission of gonorrhea.

Prepartal Infection of the Placenta with *Neisseria gonorrhoeae*

F. Yvert, E. Frost, P. Walter, R. Gass and B. Ivanoff. Genitourin Med 1985 Apr;61(2):103-5.

Placentas from 191 consecutive deliveries were cultured for *Neisseria gonorrhoeae* and other bacteria before being examined histologically. *N. gonorrhoeae* was seen on direct microscopical examination and cultured from two placentas, one of which had chorioamnionitis and the other had a granulocytic invasion of the membranes. In both patients, rupture of the membranes had occurred two hours or less before delivery, and thus after infection. A third patient was also found to have light gonococcal infection of the placenta. Six infections with group B streptococci were identified, but only one correlated with chorioamnionitis. Chorioamnionitis was observed in 16 (8.4%) and granulocytic infiltration of the membranes in 18 (9.4%) of the deliveries.

Problems of Venereal Disease in Nigeria. 1. Gonococcal Resistance to Antibiotics and Treatment of Gonorrhea

K.O. Oboho. Fam Pract 1984 Dec;1(4):219-21.

Venereal disease is becoming an increasingly serious problem in developing countries. The availability of antibiotics in chemists' shops has encouraged self-medication with sub-therapeutic doses and inadequate treatment regimens. At a health center in Nigeria, a diagnosis of gonococcal urethritis was made in 159 out of 429 men presenting with urethritis. *Neisseria gonorrhoeae* was cultured in 141 cases and the sensitivity pattern to a number of antibiotics freely available at chemists was determined. The organisms were highly resistant to penicillin (84%), ampicillin (80%), tetracycline (68%), streptomycin (78%) and co-trimoxazole (83%). These were the cheapest of the drugs available, leaving only erythromycin and the more expensive drugs gentamicin and cefotaxime still effective for general use in treatment programs.

Spontaneous Bacterial Peritonitis Caused by *Neisseria gonorrhoeae*. Evidence for a Transfallopian Route of Infection

W.N. Stassen, A.J. McCullough and P.K. Hilton. Gastroenterology 1985 Mar;88(3):804-7.

We describe the clinical and laboratory features of a case of spontaneous bacterial peritonitis caused by *Neisseria gonorrhoeae* in a sexually active woman with Laennec's cirrhosis, ascites, and asymptomatic cervical gonorrhea. Treatment of the infection with high-dose parenteral penicillin was associated with resolution of the infection. This first report of spontaneous gonococcal peritonitis provides highly suggestive evidence that the transfallopian route is a mechanism whereby bacteria may enter the peritoneal cavity. Appropriate cultures for this organism should be included when a woman with chronic liver disease, who is sexually active, presents with spontaneous peritonitis.

Single-Site Infection with *Neisseria gonorrhoeae* in Homosexual Men

B.L. Carlson and M.S. Haley. Sex Transm Dis 1984 Oct-Dec;11(4):312-3.

To determine need to culture multiple anatomic sites of homosexual men, we examined 1,803 cultures from 791 men who had positive cultures for *Neisseria gonorrhoeae* from one or more sites. The men were examined during fiscal year 1982 at a health center that serves the gay community. Not included are 184 patients who had positive cultures from the only site tested. Of the 607 patients cultured from two or more anatomic sites, 34 (5.6%) had cultures positive for *N. gonorrhoeae* from each site, and 492 (81.1%) had *N. gonorrhoeae* isolated from one site only. Of these 492 patients, 36 (7.3%) had positive cultures from the oropharynx only, 232 (47.2%) from the urethra only, and 224 (45.5%) from the anal canal only. Of 405 patients cultured from the urethra, anal canal, and oropharynx, 92 (22.7%) had *N. gonorrhoeae* at two or more sites; 313 (77.3%) had the organism at one site only. Of 84 patients cultured from the anal canal and oropharynx only, 11 (13.1%) had positive cultures from the oropharynx and negative cultures from the anal canal. Since it is highly improbable that the infected site will be selected if only one site is cultured, routine culturing of the urethra, anal canal, and oropharynx of homosexual men is necessary for accurate diagnosis.

Laboratory Diagnosis

Validity and Cost-Effectiveness of the Gonozyme Test in the Diagnosis of Gonorrhea

E. Thomas, S.D. Scott, I. Grefkees, G. Hession, R. Pollock, T. Martin and W. Albritton. Can Med Assoc J 1986 Jan 15;134(2):121-4, 146.

Although bacterial culture is considered to provide the most definitive diagnosis of gonorrhea, it has limitations when specimens must be transported long distances. A study was carried out to evaluate the validity and cost-effectiveness of an alternative method of diagnosing gonorrhea, the Gonozyme test, a commercially available enzyme immunoassay. Urogenital specimens from 100 men and 100 women with symptoms suggestive of or a history of exposure to gonorrhea were tested for the presence of *Neisseria gonorrhoeae* by means of bacterial culture and for gonococcal antigen with the Gonozyme test. The specimens from the men were also examined by means of microscopy of Gram-stained smears. The sensitivity and specificity of the Gonozyme test with reference to culture results were 95.6 percent and 97.4 percent, respectively, in the men and 84.2 percent and 98.7 percent in the women. The predictive value of a positive result was 91.6 percent in the men and 94.1 percent in the women, and the predictive value of a negative result 98.6 percent in the men and 96.3 percent in the women. The cost-effectiveness of the Gonozyme test was higher than that of bacterial culture in this population, which had a high prevalence rate of gonorrhea (23% in the men and 19% in the women). The Gonozyme test would be an adequate alternative to culture for the diagnosis of gonorrhea and contact tracing in areas far from diagnostic laboratories.

Benefit-Cost Analysis of Screening. A Comparison of Tests for Gonorrhea

J.H. Goddeeris and T.P. Bronken. Med Care 1985 Nov;23(11):1242-55.

This article develops a framework for benefit-cost analysis of screening tests and applies it to compare tests for gonorrhea in asymptomatic women. Some analytic results on the dependence of net benefits on the values of various parameters are derived. A benefit-cost analysis is then performed to compare the modified Thayer-Martin culture technique and the Gonozyme immunoassay with each other and with a no screening alternative. Analysis of the sensitivity of results to changes in assumed parameter values is also carried out. The findings suggest that the Thayer-Martin technique has positive net benefits and is preferred to Gonozyme under a broad range of plausible conditions.

Evaluation of a Modified Enzyme Immunoassay for *Neisseria gonorrhoeae* in High- and Low-Risk Females

M.R. Skeels, B. Matsuda, H. Horton, J. Sampson, G.A. Sawyer and J. Mitchell. Can J Microbiol 1985 Oct;31(10):893-5.

A recently modified commercial enzyme immunoassay (Gonozyme; Abbott Laboratories, North Chicago, IL) for *Neisseria gonorrhoeae* antigens was compared with bacteriological culture for diagnostic sensitivity, specificity, and predictive value. A total of 480 specimens were tested by both methods; 355 from females attending a sexually transmitted disease clinic ("high-risk") and 125 from female family planning clients ("low-risk"). Sensitivity and specificity of enzyme immunoassay for sexually transmitted disease clinic specimens were 79.7 and 97.9 percent, respectively (55 positive, 280 negative, 6 false positive, 14 false negative). In the low-risk population, sensitivity and specificity were 100 and 97.5 percent, respectively (3 positive, 119 negative, 3 false positive, 0 false negative). Despite modification, sensitivity of the method remains low for our sexually transmitted disease clinic population, but the test may have applicability for preliminary screening in low-prevalence settings.

Evaluation of a Direct Immunofluorescence Test for Diagnosing Gonorrhea

C.A. Ison, K. McLean, J. Gedney, P.E. Munday, D. Coghill, R. Smith, J.R. Harris and C.S. Easmon. J Clin Pathol 1985 Oct;38(10):1142-5.

A new direct immunofluorescence reagent (Syva and Genetic Systems, Inc) was evaluated for its ability to detect *Neisseria gonorrhoeae* in specimens from populations with a high prevalence of the infection. Gonorrhea was diagnosed by culture in 45 of 105 (43%) urethral specimens from men and 17 of 90 (28%) urethral and 25 of 60 (42%) cervical specimens from women. In men, the immunofluorescence test had a sensitivity of 84.4 percent and a specificity of 100 percent; Gram staining gave values of 94 percent and 100 percent, respectively. The sensitivity of the immunofluorescence test could be increased to 89 percent by testing duplicate smears. In women, the immunofluorescence test had a sensitivity of 65 percent and a specificity of 98 percent for urethral samples and values of 72 percent and 94 percent, respectively, for cervical samples. At both sites, the sensitivity of the Gram stain was 40 percent and the specificity 100 percent. The testing of duplicate immunofluorescence smears increased the sensitivity to 76 percent for urethral and 88 percent for cervical samples.

Difficulties in Differentiating *Neisseria cinerea* from *Neisseria gonorrhoeae* in Rapid Systems Used for Identifying Pathogenic Neisseria Species

J.M. Boyce and E.B. Mitchell, Jr. J Clin Microbiol 1985 Nov;22(5):731-4.

Neisseria cinerea and *Neisseria gonorrhoeae* may occur at the same body sites and may have similar colony morphologies. Ideally, systems used for rapid identification of *N. gonorrhoeae* should be able to differentiate *N. cinerea* from gonococci. We tested seven *N. cinerea* strains using the Gonochek II (Du Pont Diagnostics), Minitek (BBL Microbiology Systems), RapID-NH (Innovative Diagnostics, Inc.), RIM-N (American Microscan), and Phadebact (Pharmacia Diagnostics) systems. We found that the reactions produced by *N. cinerea* in Gonochek II, Minitek, and RapID-NH kits could be confused with the results produced by some strains of *N. gonorrhoeae*. The susceptibility of *N. cinerea* to colistin, its ability to grow on tryptic soy or Mueller-Hinton agar, and its inability to grow on modified Thayer-Martin medium help differentiate it from gonococci.

Comparison of the Effect of Refrigerated Versus Room Temperature Media on the Isolation of *Neisseria gonorrhoeae* from Genital Specimens

H.B. Ratner, H. Tinsley, R.E. Keller and C.W. Stratton. J Clin Microbiol 1985 Jan;21(1):127-8.

We evaluated the effect of medium temperature at the time of inoculation on the isolation of *Neisseria gonorrhoeae* from urethral and cervical swabs. There were no major differences in the isolation rates of 176 positive cultures on cold or warm media. Colonies tended to be larger and more numerous on room temperature plates after 24 hours; however, colonies on most refrigerated plates were easily recognized at 24 hours, and growth was essentially the same on both plates after 48 hours.

Evaluation of GonoGen Coagglutination Test for Serodiagnosis of *Neisseria gonorrhoeae:* Identification of Problem Isolates by Auxotyping, Serotyping, and with a Fluorescent Antibody Reagent

B.H. Minshew, J.L. Beardsley and J.S. Knapp. Diagn Microbiol Infect Dis 1985 Jan;3(1):41-6.

GonoGen (Micro-Media Systems, Potomac, MD) is a commercially available coagglutination test for the identification of *Neisseria gonorrhoeae*. We tested 84 strains of *Neisseria spp.* and *Branhamella catarrhalis*, including 50 clinical isolates of *N. gonorrhoeae*. Eighty-six percent (51/59) of *N. gonorrhoeae*, including 86 percent (43/50) of clinical isolates of *N. gonorrhoeae*, were identified correctly in the GonoGen test. In contrast, all *N. gonorrhoeae* isolates reacted with a fluorescent antibody research reagent composed of monoclonal antibodies. Both reagents were specific for *N. gonorrhoeae*. Clinical isolates were classified by auxotyping and were serotyped with research monoclonal antibody reagents in coagglutination tests to characterize problem isolates; two auxotype/serovar classes, prototrophic/IA-4 and proline-requiring/IA-4, accounted for 71 percent (5/7) of GonoGen-negative clinical isolates. Five of the seven isolates that were missed with the first GonoGen lot we tested did react with a second lot of GonoGen reagent. Investigators from different cities in the U.S. have reported different rates of success with GonoGen. Our results indicate that certain *N. gonorrhoeae* serovars may account for the difference in performance observed with serological tests.

Evaluation of a DNA-Hybridization Method for Detection of African and Asian Strains of *Neisseria gonorrhoeae* in Men with Urethritis

P.L. Perine, P.A. Totten, K.K. Holmes, E.H. Sng, A.V. Ratnam, R. Widy-Wersky, H. Nsanze, E. Habte-Gabr and W.G. Westbrook. J Infect Dis 1985 Jul; 152(1):59-63.

The 2.6-megadalton (MDa) cryptic plasmid and the 4.4-MDa beta-lactamase plasmid of *Neisseria gonorrhoeae* were radiolabeled with (32P) nucleotides and used as probes for direct detection of gonococci and beta-lactamase plasmids in urethral exudates from men with urethritis. The sensitivity and specificity of the DNA probes were compared with culture isolation of *N. gonorrhoeae* and biochemical tests of gonococcal isolates for beta-lactamase production. Of 216 urethral specimens, 180 were positive for *N. gonorrhoeae* by DNA probe and culture, 27 were negative by both tests, and 9 gave discordant results. Compared with culture and with the chromogenic cephalosporin assay, the sensitivity and the specificity of the DNA probe was 99 percent and 93 percent and that of the beta-lactamase probe assay was 91 percent and 96 percent, respectively. Electrophoresis of plasmids isolated from 90 gonococcal cultures showed that all contained the 2.6-MDa plasmid, 29 possessed a 3.2-MDa plasmid, 18 a 4.4-MDa beta-lactamase plasmid, and 11 had a 24.5-MDa conjugal plasmid. We conclude that the sensitivity of our DNA probes was comparable to that of culture for diagnosis of gonorrhea and to conventional tests for detection of beta-lactamase.

Comparative Evaluation of Five Commercial Systems for the Rapid Identification of Pathogenic Neisseria Species

A. Philip and G.C. Garton. J Clin Microbiol 1985 Jul;22(1):101-4.

Prompt diagnosis and effective treatment of urogenital gonococcal infections require rapid isolation and identification of *Neisseria gonorrhoeae* from urogenital specimens. We evaluated a new, rapid (30-min) test called Gonochek II (E-Y Laboratories, San Mateo, Calif.) which utilizes chromogenic substrates for the identification of pathogenic Neisseria species. It was compared with the API NeIdent (Analytab Products, Inc., Plainview, N.Y.), Minitek (BBL Microbiology Systems, Cockeysville, Md.), and RapID NH (Innovative Diagnostics, Atlanta, Ga.), systems and the Phadebact GC (Pharmacia Diagnostics, Piscataway, N.J.) test for its performance in identifying known strains of *N. gonorrhoeae* (39 strains), *Neisseria meningitidis* (22 strains), *Neisseria lactamica* (12 strains), and *Branhamella catarrhalis* (17 strains). The Gonochek II system correctly identified 100 percent of *N. gonorrhoeae*, *N. lactamica*, and *B. catarrhalis* strains and 95.4 percent of *N. meningitidis* strains. The percent agreement for correct identification of all strains tested was 98.8 percent. In contrast, the Minitek, RapID NH, and API NeIdent systems correctly identified 86.6, 80.0, and 73.3 percent of the strains, respectively. The Phadebact GC test identified 94.9 percent of the *N. gonorrhoeae* isolates but also cross-reacted with 41.6 percent of the *N. lactamica* strains. The Gonochek II system is rapid, simple to perform, and easy to interpret, requires 1 to 2 minutes to set up, and more accurately identifies pathogenic Neisseria species when compared with other systems used in this study.

Sensitivity Pattern and Beta-Lactamase Screening of *Neisseria gonorrhoeae* Strains Isolated in Zaria, Northern Nigeria

R.M. Joshi and R.V. Lawande. Trop Geogr Med 1985 Mar;37(1):74-6.

One hundred and sixty strains of *N. gonorrhoeae* were studied for their in vitro sensitivity to six different antimicrobial agents and tested for beta-lactamase production in Zaria, Northern Nigeria. While 82 percent of strains were sensitive to erythromycin, 70 percent to tetracycline and 61 percent to chloramphenicol, only 35 percent, 33 percent and 24 percent were sensitive to ampicillin, penicillin and streptomycin, respectively. Penicillin is no more the drug of choice in the treatment of gonorrhea in this environment since two thirds of strains are either partially resistant or completely resistant to penicillin and 44 percent of strains are beta-lactamase producers. Erythromycin/tetracycline are recommended as the drugs of choice.

Proctitis Associated with *Neisseria cinerea* Misidentified as *Neisseria gonorrhoeae* in a Child

J.H. Dossett, P.C. Appelbaum, J.S. Knapp and P.A. Totten. J Clin Microbiol 1985 Apr;21(4):575-7.

An 8-year-old boy developed proctitis. Rectal swabs yielded a *Neisseria sp.* that was repeatedly identified by API (Analytab Products, Plainview, N.Y.), Minitek (BBL Microbiology Systems, Cockeysville, Md.), and Bactec (Johnston Laboratories, Towson, Md.) methods as *Neisseria gonorrhoeae*. Subsequent testing in a reference laboratory yielded an identification of *Neisseria cinerea*. It is suggested that identification of a *Neisseria sp.* isolated from genital or rectal sites in a child be confirmed by additional serological, growth, and antibiotic susceptibility tests and, if necessary, by a reference laboratory. The implications of such misidentifications are discussed.

Urine as a Holding Medium for *Neisseria gonorrhoeae*

C.E. Rosey and E.M. Britt. Sex Transm Dis 1984 Oct-Dec;11(4):301-3.

An earlier technique for culturing of *Neisseria gonorrhoeae* from uncentrifuged first-voided urine from males demonstrated a sensitivity of 92-99 percent as compared with the gram stain of urethral exudate and the urethral swab culture. In this study, the utility of urine as a holding medium for *N. gonorrhoeae* was tested. Determination of a reliable minimal survival time for *N. gonorrhoeae* in urine was made by collection of 2-60 ml of first-voided urine prior to treatment from 97 men known to have genitourinary gonorrhea. The urine specimens were held at room temperature (approximately 22 C), while separate modified Thayer-Martin culture plates were inoculated from each specimen immediately after collection and at carefully timed intervals up to 48 hours afterward. *N. gonorrhoeae* was recovered from 95 percent of the urine specimens for up to 12 hours after the specimens were collected.

Therapy

Single Dose Treatment of Gonococcal Urethritis with Augmentin in Ibadan

A.O. Osoba, A.O. Oyelese, J.O. Ashiru, C.C. Ekweozor and J. Ochei. Afr J Med Med Sci 1985 Sep-Dec; 14(3-4):169-73.

Augmentin, a new orally absorbed broadspectrum antibacterial agent comprised of amoxycillin trihydrate and potassium clavulanate, was investigated in the treatment of gonococcal urethritis in Ibadan, Nigeria, where penicillinase-producing *Neisseria gonorrhoeae* (PPNG) constitutes about 80 percent of the circulating strains of gonococci. Two different formulations of the agent were employed in the study. The first formulation, consisting of 3.0 g amoxycillin and 125 mg clavulanic acid, achieved a cure rate of 75 percent (i.e., 18 out of 24 patients) among PPNG infections, but 100 percent cure rate among nine patients with non-PPNG infections. The second formulation, consisting of 3.0 g amoxycillin and 250 mg clavulanic acid, had a cure rate of 86 percent (i.e., 57 out of 66 patients) among PPNG infections, and 91 percent (i.e., 10 out of 11 patients) among non-PPNG infections. Clavulanic acid appears to potentiate and enhance the activity of amoxycillin against the beta-lactamase produced by the gonococci. Augmentin seems to be a good and acceptable agent for the treatment of gonococcal infections in this environment and further studies on its efficacy are therefore justified, such as the simultaneous administration of probenecid.

The Use of Aztreonam in the Treatment of Uncomplicated Gonorrhea

R.C. Spencer and M.D. Talbot. Curr Med Res Opin 1985;9(9):591-3.

A total of 57 men and 26 women with uncomplicated gonorrhea was treated with 1 g aztreonam intramuscularly. The cure rate was 96 percent and included successful treatment of four infections due to beta-lactamase producing organisms and eight patients with pharyngeal involvement. The minimum inhibitory concentrations of aztreonam in vitro were lower than those of penicillin and similar to cefuroxime, and side effects were minimal. It is concluded that aztreonam is effective against *Neisseria gonorrhoeae* in vivo and in vitro.

Treating Gonococcal Infections Resistant to Penicillin in Bangkok: Comparison of Cefuroxime and Spectinomycin

A. Chitwarakorn, C. Ariyarit, K. Panikabutra, A. Buateing, J. Biddle, S. Thompson and S. Brown. Genitourin Med 1985 Oct;61(5):306-10.

Gonococcal organisms have become resistant to antimicrobials throughout the world. Such resistance is common in Thailand, where 40 percent of gonococci produce penicillinase (PPNG strains) and over half the remainder have MICs of penicillin greater than or equal to 1 mg/l. To evaluate the effectiveness of cefuroxime against such resistant organisms, a controlled clinical trial comparing spectinomycin and cefuroxime was conducted at Bangrak Hospital, Bangkok, in 1982-3. Of 472 patients who were randomly assigned to treatment, 365 (77%) yielded positive cultures before treatment and returned for follow-up evaluation three to 13 days after treatment. Of the 365 patients, 359 (98%) were cured, and no difference between the two treatment regimens was found either by the sex of the patient or by the presence of PPNG strains. The MIC of cefuroxime against all organisms was less than or equal to 1 mg/l. In vitro susceptibilities of gonococci in Bangkok have not changed appreciably during the past two years. Regimens of cefuroxime and spectinomycin are highly effective even for the relatively resistant gonococci in Bangkok. The pharmacokinetics, in vitro susceptibilities, and effectiveness of cefuroxime encourage evaluation of lower doses of the drug.

Single Dose Ciprofloxacin for Treating Gonococcal Infections in Men

P.S. Loo, G.L. Ridgway and J.D. Oriel. Genitourin Med 1985 Oct;61(5):302-5.

A single oral dose of ciprofloxacin 500 mg was used to treat five men with gonococcal urethritis and five men with gonococcal proctitis, and all were cured. In a subsequent study, the dose of ciprofloxacin was reduced to 250 mg, and 54 men with 57 gonococcal infections (47 urethral, seven rectal, and three pharyngeal) were treated; of the isolates of *Neisseria gonorrhoeae*, four were penicillinase-producing strains. All the patients were cured of gonococcal infection. Urethral specimens from nine of the men with gonococcal urethritis yielded *Chlamydia trachomatis* before treatment. These organisms were isolated again from all these patients seven days after treatment, and from a further seven men who had been chlamydia negative before treatment. It is concluded that a single oral dose of ciprofloxacin is an effective treatment for uncomplicated gonorrhea, but is ineffective against *C. trachomatis*. Of the 54 men given 250 mg ciprofloxacin, six (11%) showed minor abnormalities of liver function tests after treatment.

Comparative Study of Ceftriaxone and Spectinomycin for Treatment of Pharyngeal and Anorectal Gonorrhea

F.N. Judson, J.M. Ehret and H.H. Handsfield. JAMA 1985 Mar 8;253(10):1417-9

Of the currently recommended regimens for treatment of uncomplicated gonorrhea, only aqueous penicillin G procaine is effective against infections at all sites. However, procaine penicillin is not effective against penicillinase-producing *Neisseria gonorrhoeae* and suffers from poor patient acceptability owing to the 10-mL volume of injection and allergic and toxic procaine reactions. Ceftriaxone is a new extended-spectrum cephalosporin with a long serum half-life and is many times more active than penicillin G against both beta-lactamase-positive or -negative strains of *N. gonorrhoeae*. Ceftriaxone was compared as a single, 125-mg, 0.5-mL injection with a single 2-g injection of spectinomycin in difficult to treat pharyngeal gonorrhea in men and women and anorectal gonorrhea of men. Ceftriaxone cured 30/32 (94%) pharyngeal and 52/52 anorectal infections, compared with 6/14 (43%) and 9/9, respectively, for spectinomycin. Both regimens were well tolerated. Ceftriaxone may prove to be a drug of choice for uncomplicated gonorrhea, particularly where homosexual men are treated and/or penicillinase-producing *N. gonorrhoeae* is prevalent.

A Comparison of Penicillin G Plus a Beta-Lactamase Inhibitor (Sulbactam) with Spectinomycin for Treatment of Urethritis Caused by Penicillinase-Producing *Neisseria gonorrhoeae*

S.R. Crider, M.E. Kilpatrick, W.O. Harrison, S.B. Kerbs and S.W. Berg. Sex Transm Dis 1984 Oct-Dec;11(4):314-7

When combined with penicillin, sulbactam, a beta-lactamase inhibitor with weak intrinsic antibacterial activity, produces a marked synergistic effect in vitro against penicillinase-producing *Neisseria gonorrhoeae*. We compared a regimen of aqueous procaine penicillin G, sulbactam, and probenecid with spectinomycin for the treatment of uncomplicated gonococcal urethritis. Of 101 patients receiving the penicillin-sulbactam regimen, 97 (97%) were cured of their infection, as were 87 (95%) of 92 patients who received spectinomycin. Fifty percent of patients were infected with penicillinase-producing *N. gonorrhoeae*; 43 (94%) of 46 treated with the penicillin-sulbactam regimen were cured as compared with 47 (92%) of 51 treated with spectinomycin. Neither regimen was associated with serious adverse effects. The results show that aqueous procaine penicillin G given with sulbactam and probenecid is an effective alternative for single-session therapy of urethritis caused by penicillinase-producing *N. gonorrhoeae*.

Susceptibility of *Neisseria gonorrhoeae* to Rifampicin and Thiamphenicol: Correlation with Protein I Antigenic Determinants

S.M. Bygdeman, P.A. Mcardh and E.G. Sandstrom. Sex Transm Dis 1984 Oct-Dec;11(4 Suppl):366-70

Tests of susceptibility to thiamphenicol and rifampicin were done for 85 strains of *Neisseria gonorrhoeae*, including 28 beta-lactamase-producing and three spectinomycin-resistant isolates. Strains were serogrouped by co-agglutination with 14 monoclonal antibodies that are specific for different antigenic determinants on protein I of the gonococcal outer membrane. Thus the isolates could be classified into one of the serogroups WI, WII, or WIII and could be subgrouped further into several serovars. The minimal inhibitory concentration (MIC) of thiamphenicol ranged between 0.125 and 4.0 micrograms/ml and that of rifampicin between 0.016 and 4.0 micrograms/ml. All isolates with a MIC of rifampicin of greater than or equal to 0.5 microgram/ml had a MIC of thiamphenicol of greater than or equal to 2.0 micrograms/ml. Decreased susceptibility (thiamphenicol MIC, greater than or equal to 1.0 microgram/ml; rifampicin MIC, greater than or equal to 0.5 microgram/ml) to both drugs was correlated with serogroup WII specificity and also correlated with strains that belonged to serovars characterized by a positive reaction with the WII monoclonal antibody 2G2.

Single Dose Oral Amoxycillin 3 g with Either 125 mg or 250 mg Clavulanic Acid to Treat Uncomplicated Anogenital Gonorrhea

A.G. Lawrence and D.C. Shanson. Genitourin Med 1985 Jun;61(3):168-71.

A single supervised oral dose of amoxycillin 3 g combined with clavulanic acid 125 mg as a suspension (Augmentin 3.125G) plus probenecid 1 g, cured 97 of 100 assessable patients who had uncomplicated anogenital gonorrhea. Thirteen of the 100 patients were infected with penicillinase producing strains of *Neisseria gonorrhoeae* (PPNG) and 11 (85%) of these patients were cured, including one infected with a PPNG strain that was also resistant to spectinomycin. Another group of 93 assessable patients was treated with ampicillin 3 g plus probenecid 1 g, and only 85 (91%) patients were cured. Of the eight treatment failures in this group, five were found to be infected with PPNG strains. In a second study, 144 assessable patients were treated with amoxycillin 3 g combined with clavulanic acid 250 mg, (Augmentin 3.250G) plus probenecid 1 g, and a 97 percent cure rate was again obtained. Five of seven (71%) patients infected with PPNG strains were cured. Although both Augmentin regimens were effective for treating gonorrhea caused by PPNG and non-PPNG strains, side effects were noted in more patients treated with 250 mg clavulanic acid (24%) than with 125 mg clavulanic acid (5%). In addition, a similar cure rate was obtained in the three primary sites of infection, the urethra, cervix, and rectum.

Augmentin Compared with Amoxycillin in Treating Uncomplicated Gonorrhea

P.R. Key, B.S. Azadian and B.A. Evans. Genitourin Med 1985 Jun;61(3):165-7.

We studied 220 patients (138 men and 82 women) with uncomplicated gonorrhea who were entered into a randomized double blind trial and treated with either Augmentin (amoxycillin 3 g and potassium clavulanate 125 mg) or amoxycillin 3 g, with probenecid 1 g by mouth in all cases. Seven (6.5%) of 108 patients treated with Augmentin were still culture positive after treatment, compared with 15 (13.4%) of 112 of those treated with amoxycillin. Penicillinase (beta-lactamase) producing strains of *Neisseria gonorrhoeae* (PPNG) were found in 23 (10.5%) patients, of whom 10 were treated with Augmentin and 13 with amoxycillin. Treatment failed in all 13 patients who received amoxycillin. Augmentin was shown to be an effective treatment for gonorrhea caused by PPNG strains.

Effect of Amoxicillin on Simultaneous *Chlamydia trachomatis* Infection in Men with Gonococcal Urethritis: Comparison of Three Dosage Regimens

P.A. Csango, T. Gundersen and I.M. Martinsen. Sex Transm Dis 1985 Apr-Jun;12(2):93-6.

Of 92 men with gonococcal urethritis who were treated orally with amoxicillin, 25 (27.1%) had a simultaneous *Chlamydia trachomatis* infection. At the first visit, 25 patients were treated with a single dose of 1 g of amoxicillin plus 1 g of probenecid (group 1); 24 men were treated with 1 g of amoxicillin twice a day for two days (group 2); and 43 men were treated with 0.75 mg of amoxicillin three times a day for seven days (group 3). At the follow-up visit, one patient in each group still had *Neisseria gonorrhoeae*-positive cultures. *C. trachomatis* was not isolated again after treatment from men in group 3, but was isolated from 81.8 percent in groups 1 and 2 combined (P less than 0.05). One (10%) of the ten men in group 3 who were *C. trachomatis*-positive before treatment developed postgonococcal urethritis, as compared with seven (63.6%) of 11 in groups 1 and 2 combined (P less than 0.05). Thus a multiple-dose amoxicillin regimen may prove to be a useful alternative to the present-day treatment of chlamydial infections of the urogenital tract.

Treatment of Uncomplicated Gonorrhea in Women with Single-Dose Cefonicid

H.H. Handsfield and V.L. Murphy. Sex Transm Dis 1985 Apr-Jun;12(2):90-2.

The efficacy of cefonicid (1.0 g given in a single intramuscular dose) was assessed in 50 women with uncomplicated infections due to beta-lactamase-negative strains of *Neisseria gonorrhoeae*. Forty-three (96%) of 45 cervical infections, but only 23 (82%) of 28 anorectal infections, were eradicated; overall, 44 (90%) of 49 women were cured of anogenital gonorrhea. Cefonicid failed to eradicate six (55%) of 11 pharyngeal gonococcal infections and 17 (85%) of 20 endocervical infections with *Chlamydia trachomatis*. Cefonicid had good activity against *N. gonorrhoeae* in vitro; 41 (98%) of 42 isolates were inhibited by less than or equal to 1.0 micrograms/ml. However, because of its poor efficacy against anorectal and pharyngeal gonococcal infections, single-dose cefonicid is not suitable for the treatment of gonorrhea in women or homosexually active men.

Randomized Comparative Study of Ceftriaxone and Spectinomycin in Gonorrhea

K. Panikabutra, C. Ariyarit, A. Chitwarakorn, C. Saensanoh and C. Wongba. Genitourin Med 1985 Apr;61(2):106-8.

From April 26 to June 30, 1983 a total of 200 men with uncomplicated gonococcal urethritis were randomly treated with either 2 g spectinomycin or 250 mg ceftriaxone, both administered intramuscularly. Of 197 isolates tested for the presence of the enzyme beta lactamase, 91 (46.2%) were positive (PPNG) and 106 (53.8%) were non-PPNG strains. All 93 patients treated with spectinomycin and followed up and 97 treated with ceftriaxone and followed up were cured. Ceftriaxone 250 mg administered by intramuscular injection is highly effective in treating gonococcal infections caused by both PPNG and non-PPNG strains and is an appropriate alternative to spectinomycin.

Effectiveness of Aztreonam for the Treatment of Gonorrhea

A. Gottlieb and J. Mills. Antimicrob Agents Chemother 1985 Feb;27(2):270-1.

Aztreonam, 1 g intramuscularly, was compared with spectinomycin, 2 g intramuscularly, for uncomplicated gonorrhea. There were no failures with either drug. For aztreonam, there were 26 urethral, 3 rectal, and 3 endocervical sites that were infected. Aztreonam in a single dose of 1 g intramuscularly is satisfactory therapy for uncomplicated urethral gonorrhea in men and may be effective for rectal and endocervical infection as well.

Clinical Trial of Thiamphenicol Therapy for Uncomplicated Gonorrhea

C.S. De Parra, H.L. Cortes and J.S. Medina. Sex Transm Dis 1984 Oct-Dec;11(4 Suppl):423-5.

The need for a safe drug that is easy to administer and not too expensive prompted a study of treatment of uncomplicated gonorrhea with a single oral dose of 2.5 g of thiamphenicol. Of 169 patients treated, 161 were cured. Of the 92 patients with acute infections, all of the 13 men and 74 (93.7%) of the 79 women were cured. Seventy-seven cases were defined as reinfection; all of the 22 men in this group were cured, as were 52 (94.5%) of the 55 women. Only minor adverse effects were noted. It is concluded that thiamphenicol is a safe and effective antibiotic for therapy of uncomplicated gonorrhea.

Single-Dose Treatment of Uncomplicated Gonorrhea: A Comparison of Cefonicid and Penicillin

W.C. Duncan and M.E. McBride. Rev Infect Dis 1984 Nov-Dec;6 Suppl 4:S875-9.

Cefonicid, a parenteral semisynthetic cephalosporin, achieves high and sustained serum levels in humans. Activity against strains of *Neisseria gonorrhoeae*, including those that produce beta-lactamase, has been shown in vitro. The efficacy of 1.0 g of cefonicid was evaluated noncomparatively in 50 men with gonococcal urethritis; four failed to respond to treatment. Additionally, 57 men and 34 women received either 1.0 g of cefonicid or 4.8 X 10(6) units of procaine penicillin G plus 1.0 g of probenecid in a double-blind study. Among 17 men treated with penicillin, two failed to respond, and one failed among the 33 patients treated with cefonicid. Seventeen women received 1.0 g of cefonicid, and all cervical infections were cured. Among those who received cefonicid, 13 had rectal infections; and four had positive cultures at follow-up four to seven days posttreatment. Among the 17 women receiving penicillin, none failed to respond to therapy; only seven had both cervical and rectal infection. Of the 116 pretreatment and seven posttreatment isolates tested, 45 (37%) were inhibited by less than 0.0625 microgram of penicillin/ml and 121 (98%) were inhibited by less than 1.0 microgram/ml. Forty-one (33%) of the 123 isolates were inhibited by less than 0.0625 microgram of cefonicid/ml and 122 (99%) by less than 1.0 microgram of cefonicid/ml. The median MIC of cefonicid for the strains isolated from the women whose rectal infections were cured was 0.125 microgram/ml; that for the strains isolated from the women with rectal infections who failed to respond was 0.5 microgram/ml. Administration of 1.0 g of cefonicid intramuscularly is effective therapy for uncomplicated gonococcal urethritis in men.

Comparison Between Bacampicillin and Amoxycillin in Treating Genital and Extragenital Infection with *Neisseria gonorrhoeae* and Pharyngeal Infection with *Neisseria meningitidis*

L.D. Edwards and T. Gartner. Br J Vener Dis 1984 Dec;60(6):380-3.

Sixty-three patients presumed to have genital gonorrhea, who gave histories of extragenital sexual practices, were randomly treated with amoxycillin 3 g or bacampicillin 4.8 g (equivalent to 3.5 g ampicillin) with probenecid 1 g to compare the efficacy of the drugs in treating gonorrhea at all sites. Three patients were initially culture negative, and seven failed to return for follow-up. Twenty-seven of 28 patients receiving bacampicillin and all 25 receiving amoxycillin gave negative genital cultures for *Neisseria gonorrhoeae* five to nine days after treatment. Twenty-two of 60 patients had extragenital gonorrhea. One failed to return, but all eight who had received amoxycillin and 12 of 13 who had received bacampicillin gave negative pharyngeal and anorectal cultures after treatment. *N. meningitidis* was isolated from the pharynx in 17 of 60 patients on initial attendance. Three of 14 were still colonized with the meningococcus after treatment. Two of 32 patients receiving amoxycillin and 12 of 31 receiving bacampicillin reported experiencing gastrointestinal side effects.

Treatment of *Neisseria gonorrhoeae* Infections in Men with Single-Dose Thiamphenicol

J.D. Oriel, P. Loo and D. Felmingham. Sex Transm Dis 1984 Oct-Dec;11(4 Suppl):410-3.

A group of 50 men with uncomplicated gonococcal infections were treated with single, oral doses of 2.5 g of thiamphenicol. Reexamination, which included culture for *Neisseria gonorrhoeae*, was performed three to four days and seven days after treatment. Thirty-two (91%) of 35 men with urethral infections, 13 (87%) of 15 with rectal infections, and four (57%) of seven with pharyngeal infections were cured. None of the men from whom *N. gonorrhoeae* was reisolated admitted further sexual exposure. Treatment failure did not correlate with decreased sensitivity of the isolates to thiamphenicol in vitro. Three men had urethral infections with *Chlamydia trachomatis* before therapy, and the organism was reisolated after therapy in every case. No hematologic abnormalities occurred in any of the 50 patients treated with thiamphenicol, but 13 (26%) developed adverse gastrointestinal symptoms.

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Genital Herpes Infection

Clinical

Genital Herpes: An Increasing Problem?

D.J. Hindley and M.W. Adler. Genitourin Med 1985 Feb;61(1):56-8.

Over the past 10 years there has been a pronounced increase in the number of cases of genital herpes seen in sexually transmitted disease (STD) clinics in the United Kingdom. The reporting system, however, does not differentiate between primary and recurrent infections, and consequently any increase in the number of patients reattending clinics with recurrent genital herpes would falsely inflate the statistics. A study of cases of herpes seen in the department of genitourinary medicine of this hospital in the two years 1972 and 1982 is presented. It showed that the proportion of patients attending with recurrent herpes had increased from 18 percent in 1972 to 31 percent in 1982. As a result of this, the 68 percent increase between 1972 and 1982 in the total number of cases of herpes seen in the clinic overestimates the real increase in the size of the problem, which is closer to 40 percent, based upon cases of primary herpes only. Modifications to the national recording system are necessary to overcome the problems highlighted by this study. These modifications could include classifying each case of genital herpes as primary, recurrent, or recurrent but not previously recorded, which would provide a more accurate picture of the size of the problem of genital herpes in the population.

Sites of Multiple Lesions in Recurrent Genital Herpes

W.H. Wickett, Jr. and R.D. Miller. Am Fam Physician 1985 Nov;32(5):145-52.

The location of herpes lesions affects the potential for infection of sexual partners and newborn infants. During a six-month study of more than 100 patients, 60 percent of the women and 55 percent of the men had as many as six different lesion sites, both genital and extragenital. Multiple outbreaks of lesions may occur simultaneously, or lesions may form at different times during the same recurrence. These are often inconspicuous and usually go undetected.

Coping and Adjustment to Genital Herpes

S. Manne and I. Sandler. J Behav Med 1984 Dec;7(4):391-410

The current study examined how individuals deal with genital herpes, a recurrent, incurable disease with a great psychological impact. An assessment battery composed of cognitive and problem-focused coping, attribution, and social support mechanisms was employed. These coping mechanisms were correlated with measures of psychological adjustment: self-esteem, depression, sexual adjustment, and amount upset by herpes. Subjects were 152 people with herpes recruited from self-help groups and people from the community who volunteered to participate in the study. Results supported several hypotheses derived from previous research on coping with life stressors. Cognitive coping mechanisms, especially negative thoughts, along with wishful thinking and characterological self-blame, were significant predictors of poor psychological adjustment. In addition, the repeated use of disease management strategies was found to correlate with poor psychological adjustment. Further research in the area of coping with chronic illness is suggested.

Herpes Gestationis. Persistent Disease Activity 11 Years Postpartum

J.D. Fine and E.F. Omura. Arch Dermatol 1985 Jul;121(7):924-6.

A patient had herpes gestationis that had persisted for over 11 years postpartum despite aggressive therapy with corticosteroids, dapsone, and various immunosuppressants. Postpartum exacerbation is a characteristic feature of herpes gestationis. However, it usually is of short duration and is responsive to conventional therapy.

Incidences of Antibodies to Hepatitis B, Herpes Simplex and Cytomegalovirus in Prostitutes

B. Dannenmaier, W. Alle, E.W. Hoferer, D. Lorenz, P.J. Oertel and H.W. Doerr. Zentralbl Bakteriol Mikrobiol Hyg (A) 1985 Apr;259(2):275-83.

The 170 prostitutes registered by the local public health authority (165 female, 5 male; ages 17-61) were serologically investigated by ELISA and CFT for the presence of hepatitis B virus (HBV) markers (n = 170), anti-CMV (n = 118) and anti-HSV 2 antibodies (n = 117). Of the group, 4.7 percent (1.2%) were found to be HBs-(HBe-)antigen carriers; 1.2 percent revealed an acute hepatitis B (seroconversion of anti-HBc or IgM-anti-HBc highly positive); 17.1 percent presented a past and resolved hepatitis B (anti-HBs positive). These rates exceeded those of 125 female age-matched control persons considerably, out of whom only 2.4 percent (0.8%) presented HBs−(HBe−) antigen and 3.2 percent anti-HBs antibodies. Ninety percent of the prostitutes investigated proved to be anti-CMV IgG (1.7% IgM) antibody positive and were compared to healthy blood donors (47% IgG, 0% IgM-anti-CMV antibody carriers) and other CMV risk groups: pregnant women 56 (13), patients in hemodialysis 61 (0), hemophiliac patients 69 (0), patients after kidney transplantation 90 (16) and after open-heart surgery 87 (4) percent anti-CMV IgG (IgM) antibody carriers. An AIDS patient suffered from simultaneous HBV and CMV infections. The risk of HSV 2 infection is among prostitutes (38.5% seropositives) five times as high as among female age-matched control persons (7.2% seropositives, n = 125). These results confirm that prostitutes must be regarded as a risk for the spread of hepatitis BV and CMV- and HSV 2-caused diseases in the population.

Frequency of Acquisition of First-Episode Genital Infection with Herpes Simplex Virus from Symptomatic and Asymptomatic Source Contacts

G.J. Mertz, O. Schmidt, J.L. Jourden, M.E. Guinan, M.L. Remington, A. Fahnlander, C. Winter, K.K. Holmes and L. Corey. Sex Transm Dis 1985 Jan-Mar;12(1):33-9.

Sixty-six source contacts of index patients with first-episode genital infection caused by herpes simplex virus (HSV) were evaluated for evidence of current or past HSV infections. Forty-three source contacts (65%) reported a history consistent with previous recurrent HSV infection or were experiencing a first episode of genital herpes when initially examined. However, 60 percent of these 43 contacts were not aware that they had transmissible HSV infection. Twenty-nine (67%) of the 43 individuals had had recent sexual contact with an index patient when lesions were present. All of the remaining 23 source contacts, who were without a history of symptoms consistent with HSV infection, had detectable neutralizing antibody to HSV; HSV type 2 was isolated from the cervix of two of these asymptomatic source contacts. Efforts to identify individuals with undiagnosed genital herpes and to instruct these individuals concerning the risk of disease transmission in the presence of lesions are needed if the rate of transmission is to be decreased; however, methods designed to decrease the rate of transmission by asymptomatic individuals must also be evaluated.

A Prospective Study of Herpes Simplex Virus Infection in a Defined Population in Houston, Texas

K. Adler-Storthz, G.R. Dreesman, R.H. Kaufman, J.L. Melnick and E. Adam. Am J Obstet Gynecol 1985 Mar 1;151(5):582-6.

A seroepidemiologic study was conducted to determine the incidence of antibodies to herpes simplex virus in a population of middle-class Caucasian women. In utero exposure to diethylstilbestrol did not influence the frequency of herpes simplex virus infection. The frequency of infection increased with age and number of sex partners and a 50 percent increase in incidence of herpes simplex virus type 2 infection was noted during the 4-year period of the study. Subclinical herpes simplex virus type 2 infections apparently occurred in some women without preexisting antibodies to herpes simplex virus type 1.

Genital Herpes Infections in Private Practice in the United States, 1966 to 1981

T.M. Becker, J.H. Blount and M.E. Guinan. JAMA 1985 Mar 15;253(11):1601-3.

We analyzed data on genital herpes infections in the United States from 1966 to 1981 collected by the National Disease and Therapeutic Index survey. The number of private physician-patient consultations for genital herpes increased tenfold during this period. The number of patient visits for newly diagnosed infections increased 7.5-fold. Women aged 20 to 24 years and men aged 25 to 29 years were more likely to consult a private physician for genital herpes than were patients in other age brackets. Our analysis suggests an increasing national incidence of genital herpes infections and supports the concept that genital herpes infections are epidemic in the United States.

A Case of Fulminant Herpes Simplex Hepatitis in an Adult

H. Luchtrath, V. Totovic and F. de Leon. Pathol Res Pract 1984 Nov;179(2):235-41.

The case presented documents HSV hepatitis in a 41-year-old caucasian male with a history of prolonged steroid treatment and recent irradiation for brain tumor recurrence. The fulminant nature of the hepatitis, accompanied by gastric ulcer hemorrhage, lead to his death within 24 hours of symptomatic manifestation. The diagnosis of HSV hepatitis was made postmortem. The etiology of the hepatitis was established by light microscopic identification of Cowdry type A intranuclear inclusion bodies, electron microscopic identification of virus particles, and the immunohistochemical detection of herpes simplex virus antigens.

Laboratory Diagnosis

Humoral Immune Response to HSV-1 and HSV-2 Viral Proteins in Patients with Primary Genital Herpes

R. Ashley, J. Benedetti and L. Corey. J Med Virol 1985 Oct;17(2):153-66.

The humoral immune response to HSV-1 and HSV-2 proteins was examined in patients with primary first-episode genital herpes. Ten patients had culture-proven HSV-1 infections, 37 had HSV-2 infections, and all were seronegative to HSV proteins before developing their infections. Development of serum antibodies to individual HSV proteins and glycoproteins was determined by immunoprecipitation of radiolabeled HSV-1- and HSV-2-infected cell proteins and subsequent gel electrophoresis. In HSV-1 patients, a sequential development of antibodies to HSV-1 proteins was observed with early appearance of antibodies to the nucleocapsid protein p148 and to glycoproteins gB and gC. Seroconversion to gD and to a polypeptide of 88,000 molecular weight (p88) occurred next, and, finally, seroconversion to gE and to a nonglycosylated 66,000 dalton protein p66. In HSV-2 patients, antibodies to HSV-2 proteins p148, gB, and p88 appeared within 1 week of onset of symptoms. Seroconversion to p66, gD, and to a complex of glycoproteins gC and gE ("g80") occurred later, at a mean time of approximately 3 weeks. Seroconversion to HSV-1 gB, p88, and p66 occurred significantly later than seroconversion to the homologous counterparts. Seroconversion within 21 days of onset to HSV-2 gD, g80, and p66 was associated with a longer time to the first recurrence in HSV-2 patients, suggesting a possible role of these antibodies, alone or in combination, in the maintenance of HSV-2 latency in humans.

Comparison of an Avidin-Biotin Immunoassay with Three Commercially Available Immunofluorescence Kits for Typing of Herpes Simplex Virus

D.L. Barnard, F.B. Johnson and D.F. Richards. J Clin Pathol 1985 Oct;38(10):1158-62.

An avidin-biotin complex system was compared with three commercially available immunofluorescence kits for serotyping herpes simplex virus isolates from clinical specimens. Sensitivity values showed that the Electro-Nucleonics and Immulok reagents were useful in detecting the presence of virus, whereas the predictive values showed that the Syva and Immulok reagents possessed adequate discrimination between the herpes simplex virus serotypes. The avidin-biotin complex system was equal or superior to the immunofluorescence reagents tested both in detecting herpes simplex virus antigens in cell culture and in serotyping herpes simplex virus isolates.

Diagnosis of Genital Herpes Simplex Virus Infections

L. Corey. J Reprod Med 1985 Mar;30(3 Suppl):262-8.

Genital herpes simplex virus (HSV) infections have increased markedly in the last ten years. The clinical distinction between HSV and other infectious and noninfectious causes of genital ulcer can be difficult. As such, laboratory confirmation of HSV infection should be used for all women who present with ulcerative or clinically atypical genital lesions. Isolation of the virus in tissue culture remains the gold standard for the laboratory diagnosis of HSV infections. However, many new diagnostic methods of detecting HSV antigens in clinical specimens have been developed. Those procedures appear most useful in specimens taken from genital lesions, and at present they are unproven as reliable methods of obstetric management. Serologic methods can be useful in detecting past HSV infection; however, serodiagnosis is a less sensitive and timely procedure in patients with acute HSV infection.

Detection of Herpes Simplex Infection in Cytologic Smears

S. Kapur, K. Patterson and R. Chandra. Arch Pathol Lab Med 1985 May;109(5):464-5.

We compare the results of direct immunofluorescence (IF) with cytology (Papanicolaou's stains) for diagnosis of herpes simplex infection. Thirty smears were examined. Yellow-green fluorescence was seen in 17 smears. Only eight of these smears had diagnostic cytology, and nine of the smears with positive fluorescence had none (four) to minimal (five) cytologic changes, suggesting that direct IF is a much more sensitive method for diagnosis of herpes simplex infection in cytologic smears.

Evaluation of a Commercial Enzyme-Linked Immunosorbent Assay for the Detection of Herpes Simplex Virus

D.L. Sewell and S.A. Horn. J Clin Microbiol 1985 Mar;21(3):457-8.

A total of 136 specimens were tested for the presence of herpes simplex virus by routine tissue culture and a commercial enzyme-linked immunosorbent assay (Ortho Diagnostic Systems, Inc.). Forty-six (33.8%) of the specimens were positive by tissue culture. The sensitivity and specificity of the commercial system were 69.6 and 93.3 percent, respectively. The commercial system was rapid and moderately specific but lacked the sensitivity necessary for direct specimen testing.

Comparison of Western Blot Analysis to Microneutralization for the Detection of Type-Specific Herpes Simplex Virus Antibodies

D.I. Bernstein, E. Garratty, M.A. Lovett and Y.J. Bryson. J Med Virol 1985 Mar;15(3):223-30.

A newly developed system employing separated herpes simplex virus (HSV) polypeptides electrophoretically transferred to nitrocellulose paper, Western Blot Analysis (WBA), was compared to microneutralization (MN) for the detection of type-specific antibody to HSV types 1 and 2 in 98 human sera. Sera containing HSV1-specific antibodies reacted at least twofold more densely (as quantitated by densitometric scanning) to HSV1 than HSV2 polypeptides, while sera with HSV2-specific antibodies reacted twofold more densely to HSV2 polypeptides. The reliability of this system was determined (1) by analysis of sera from patients with true primary herpes simplex infections, (2) by adsorption studies that removed cross-reacting antibodies, and (3) by comparison with neutralization. Of 36 sera found to have HSV1-type-specific antibody by WBA, 83 percent had MN ratios of less than 85 (indicating HSV1 antibody), while of 28 sera found to have HSV2-type-specific antibody by WBA, 89 percent had MN ratios of greater than 85 (indicating HSV2 antibodies). The MN ratio obtained on sera felt to have both HSV1-type-specific and HSV2-type-specific antibody by WBA ranged from 67 to 160. WBA agreed more closely with clinical isolates and adsorption studies than MN. This system not only accurately determines the HSV-type-specific antibody status of patients but provides important information on the specific immunogenic proteins.

Detection and Serotyping of Herpes Simplex Virus in MRC-5 Cells by Use of Centrifugation and Monoclonal Antibodies 16 Hours Postinoculation

C.A. Gleaves, D.J. Wilson, A.D. Wold and T.F. Smith. J Clin Microbiol 1985 Jan;21(1):29-32.

Monoclonal antibodies (Syva Co., Palo Alto, Calif.) were used for the detection and serotyping of herpes simplex virus (HSV) isolates by immunofluorescence 16 hours after inoculation of MRC-5 monolayers in 3.7-ml shell vials and after low-speed centrifugation. A total of 119 specimens were inoculated into conventional tube cell cultures and shell vials. Of 98 specimens inoculated on the same day of receipt in the laboratory (fresh specimens), all 23 (23.5%) HSV-positive specimens were identified by serotype in 16 hours in shell vials by immunofluorescence, whereas only 8 of 23 HSV-positive specimens (34.8%) produced cytopathic effects in conventional tube cell cultures in this time period. Similarly, of 21 original specimen extracts previously determined to be culture positive for HSV (stored specimens), all were detected and serotyped by the immunofluorescence test with monoclonal antibodies 16 hours postinoculation compared with the recognition of only 8 of these isolates (38.1%) by cytopathic effect that soon. This technique of centrifugal inoculation of HSV in shell vials containing MRC-5 cells permitted detection of this virus in all positive specimens with serotype determination within 16 hours postinoculation.

Therapy

Acyclovir Prophylaxis of Recurrent Genital Herpes: Randomized Placebo Controlled Crossover Study

G.R. Kinghorn, M. Jeavons, M. Rowland, I. Abeywickreme, I.G. Barton, C.W. Potter and E.A. Hickmott. Genitourin Med 1985 Dec;61(6):387-90.

Forty patients were entered into a randomized placebo controlled crossover study to assess the efficacy and safety of oral acyclovir 200 mg four times a day in the prophylaxis of recurrent genital herpes. Each treatment began during a recurrence and continued for a maximum of 84 days or until the onset of the next recurrence, when the alternate medication was started. Of 28 patients who completed both treatment courses, only three developed a recurrence while taking acyclovir compared with 26 while taking placebo. The mean time to first recurrence was more than 84 days in patients receiving acyclovir and 24 days in patients receiving placebo (p less than 0.001). The mean time to first recurrence after treatment with acyclovir ceased was 16 days. Adverse events, though thought unlikely to be related to treatment, necessitated the withdrawal from the study of two patients while taking acyclovir and one patient while taking placebo. No clinically important effects on hematological or biochemical variables occurred during the acyclovir treatment. All viral isolates tested after treatment remained sensitive to acyclovir. Acyclovir prophylaxis of recurrent genital herpes is effective and safe but does not appear to influence the natural history of the disease after cessation of 84 days' continuous treatment.

Treatment of Recurrent Genital Herpes Simplex Infections with Oral Acyclovir

M. Ruhnek-Forsbeck, E. Sandstrom, B. Andersson, G. Eriksson, K. Hersle, G.B. Lovhagen, H. Mobacken, L. Hillstrom and L. Svensson. J Antimicrob Chemother 1985 Nov;16(5):621-8.

A total of 113 patients with recurrent genital herpes were enrolled in a multicenter cross-over study. Two consecutive recurrences were treated with either oral acyclovir 200 mg or matching placebo five times daily for five days. Acyclovir significantly reduced the time to crusting and healing and the duration of new lesions and symptoms. Acyclovir was not found to have any clinically significant effect on the hematological or biochemical parameters measured, or to have caused adverse events and was well tolerated. Early self-initiated treatment may abort a recurrent attack of genital herpes without progression to the ulcerative or crusting stage.

Risk of Recurrence after Treatment of First-Episode Genital Herpes with Intravenous Acyclovir

L. Corey, A. Mindel, K.H. Fife, S. Sutherland, J. Benedetti and M.W. Adler. Sex Transm Dis 1985 Oct-Dec;12(4):215-8.

To determine whether intravenous acyclovir treatment for a first episode of genital herpes could prevent or reduce subsequent recurrences, we combined and analyzed the results of two independently conducted, randomized, double-blind, placebo-controlled studies. Sixty-one patients were enrolled in the two trials; 30 received the drug, and 31 received placebo. At entry, the demographic, epidemiologic, and clinical features of acyclovir- and placebo-treated patients from the two centers showed no significant differences. The median time to the first recurrence and the frequency of recurrences showed no significant differences when acyclovir and placebo recipients infected with either herpes simplex virus type 1 (HSV-1) or herpes simplex virus type 2 (HSV-2) were compared. However, irrespective of treatment, the median time to the first recurrence was significantly longer (293 days vs. 69 days; P less than .02) and the frequency of recurrence significantly less (0.11 recurrences per month vs. 0.43 recurrences per month; P less than .01) among patients with HSV-1 infection as compared with those who had HSV-2. It is concluded that, in patients with first-attack genital herpes, the type of HSV is the most important determinant of subsequent recurrences and that intravenous acyclovir has little effect on subsequent recurrences.

Recurrent Genital Herpes Suppressed by Oral Acyclovir: A Multicenter Double Blind Trial

R.N. Thin, D.J. Jeffries, P.K. Taylor, O.P. Ayra, P. Rodin, J. Yeo and A.P. Fiddian. J Antimicrob Chemother 1985 Aug;16(2):219-26.

Eighty-eight of 111 patients with frequently recurring genital herpes attending five centers completed a randomized, double-blind, cross-over trial with 200 mg oral acyclovir four times daily for 84 days before or after a similar course of placebo tablets. During the course of placebo, 77 (88%) patients reported the development of lesions, four (5%) the development of symptoms and/or erythema but no further signs of a recurrence and seven (8%) remained entirely free of symptoms and signs. In contrast, during acyclovir therapy, only 11 (13%) patients reported lesions, a further 37 (42%) the development of symptoms and/or erythema only, while 40 (45%) patients remained entirely free of symptoms and signs. For each parameter, the difference between active and placebo treatments was highly significant (P less than 0.001). Median times to recurrence after the end of both courses were similar. The drug was well tolerated and the findings indicate that continuous oral acyclovir therapy has a place in the management of frequent recurrences of genital herpes, though the indications are not entirely clear. One possibility is the suppression of recurrence at times when it would be especially unwelcome such as during examinations or holidays.

Alteration of Lymphocyte Transformation Response to Herpes Simplex Virus Infection by Acyclovir Therapy

W.E. Lafferty, L.A. Brewer and L. Corey. Antimicrob Agents Chemother 1984 Dec;26(6):887-91.

To evaluate the effect of acyclovir (ACV) therapy on the cellular immune response, we sequentially followed 43 patients with culture-proven first episodes of genital herpes simplex virus (HSV) infection. Twenty-three patients who were treated with ACV and 20 who received placebo had blood obtained weekly during the first 6 weeks after onset of lesions and had their in vitro lymphocyte transformation (LT) response to inactivated HSV antigens measured. The mean stimulation index to HSV antigens at week 3 among patients treated with systemic ACV was 3.5 +/− 0.64 compared to 18.4 +/− 6.89 in their placebo-treated counterparts (P less than 0.05). The mean time to the development of the peak LT response to HSV antigens was 4.3 weeks in systemic-treated versus 3.4 in placebo-treated patients (P less than 0.05). The time to the development of the peak in vitro LT response to HSV antigens and the height of that response were, however, similar between topical ACV- and topical placebo-treated patients. The geometric mean HSV-2-neutralizing titer in convalescent sera was 5.4 in recipients of systemic ACV compared to 10.0 in patients treated with systemic placebo (P less than 0.05). The LT response to HSV antigen was also measured at the first recurrence in 11 patients. No differences were found in the time to first recurrence, lesion duration, number of lesions, or mean stimulation index response to inactivated HSV antigens between the six patients treated with systemic ACV during their primary episode and the five given placebo during their primary episode. Systemic ACV therapy appears to diminish the peak in vitro LT response to inactivated HSV antigens as well as to delay the time to development of that peak response. However, the cell-mediated immune response to subsequent episodes appears similar.

The Carbon Dioxide Laser in the Treatment of Vulvar Disease

R.H. Kaufman and E.G. Friedrich, Jr. Clin Obstet Gynecol 1985 Mar;28(1):220-9.

Our review of the current use of the carbon dioxide laser in treating vulvar disease reveals that it holds significant promise in the treatment of vulvar intraepithelial carcinoma, *Condylomata acuminata*, and focal vestibular adenitis. The long-range results of such treatment, however, are not yet known. Until sufficient data are accumulated to demonstrate the efficacy of the laser in treating the vulvar dystrophies and herpes genitalis, it should be used with caution, and the results should be carefully evaluated and reported.

Systemic Acyclovir in Pregnancy: A Case Report

L. Grover, J. Kane, J. Kravitz and A. Cruz. Obstet Gynecol 1985 Feb;65(2):284-7.

Disseminated herpes simplex infection in pregnancy presents serious risk to mother and fetus. Although an uncommon problem, the high maternal and fetal mortality and morbidity accompanying disseminated herpes infection warrants aggressive new treatment. Specific antiviral chemotherapy is now possible for selected cases. The present report describes the use of acyclovir during the third trimester for disseminated herpes simplex infection. The treatment protocol used and pregnancy outcome are described for this case. Acyclovir therapy and potential toxicities are described.

Oral Acyclovir Suppression of Recurrent Genital Herpes: A Double-Blind, Placebo-Controlled, Crossover Study

A.M. Halsos, O.P. Salo, A. Lassus, E.A. Tjtta, T. Hovi, B.O. Gabrielsen and A.P. Fiddian. Acta Derm Venereol (Stockh) 1985;65(1):59-63.

A randomized, double-blind, placebo-controlled, crossover study was conducted in 31 male patients with a history of frequently recurrent genital herpes who received consecutively 200 mg acyclovir and matching placebo by mouth four times a day for 12 weeks each. During acyclovir therapy, recurrences were completely prevented in 24 (77%) and were reduced in both frequency and duration in the remainder compared with those occurring during treatment with placebo. The incidence and nature of adverse events reported during each treatment period was virtually identical. No long-term effects on recurrence rates were discernible, but chronic suppressive therapy can be considered to offer the means of controlling the severe forms of disease experienced by some patients.

Research and Evaluation

Clinical Efficacy of a Herpes Simplex Subunit Vaccine

R. Cappel, S. Sprecher, F. De Cuyper and J. De Braekeleer. J Med Virol 1985 Jun;16(2):137-45.

A DNA-free herpes simplex type 2 subunit vaccine was administered to 18 volunteers without past evidence of herpes simplex type 1 (HSV 1) or herpes simplex type 2 (HSV 2) infection, to 44 patients with severe recurrent genital HSV 2 infection, and to 15 patients with severe oral type 1 HSV recurrences. The vaccine elicited both humoral and cell-mediated immunity in 97 percent of the subjects without past HSV infections and boosted significantly the cell-mediated immunity and antibody titers in almost all the patients with recurrent HSV 1 or HSV 2. The vaccine elicited particularly the production of complement-dependent cytotoxic antibodies in 96 percent of the patients with recurrent HSV 2 infections. This might, at least partly, explain the clinical efficacy of the vaccine. Indeed, we observed a significant decrease (t test, p less than 0.01) in the attack rate of the recurrences and also a significant shortening of the time needed to complete healing of the lesions (t test, p less than 0.01).

Control of Herpes Simplex Virus Infections of the Genital Tract by Vaccination

A. Buchan, G.R. Skinner, A. Fuller, C. Hartley, J. Hallworth, D. Stocker, J. Melling and C. Wiblin. Vaccine 1985 Mar;3(1):49-53.

The apparent increasing incidence of herpes simplex virus infections of the genital tract has focused attention on the efficacy of vaccination in preventing infection or modifying established disease. Results of an 'open trial' using a DNA-free inactivated virus subunit vaccine have shown that vaccination of subjects at risk of contracting infection from their sexual partner reduced the transmission rate from 34 percent in unvaccinated controls to 0.5 percent. In a separate study, vaccination of patients who had experienced their first overt attack of herpes genitalis (the initial clinical episode) had significantly fewer recurrences over the follow-up period of 12 months than the unvaccinated control group. The results, we feel, justify a placebo controlled trial.

Protection from Genital Herpes Simplex Virus Type 2 Infection by Vaccination with Cloned Type 1 Glycoprotein D

P.W. Berman, T. Gregory, D. Crase and L.A. Lasky. Science 1985 Mar 22;227(4693):1490-2.

Guinea pigs were vaccinated with truncated herpes simplex virus type-1 (HSV-1) glycoprotein D produced in the genetically engineered mammalian cell line gD10.2. Vaccinated animals formed antibodies that neutralized both HSV-1 and herpes simplex virus type 2 (HSV-2) in an in vitro neutralization assay. Vaccinated animals were challenged with HSV-2 by intravaginal infection. Animals that received the immunogen in Freund's complete adjuvant were completely protected from the clinical manifestations of genital HSV-2 infection. Animals that received the immunogen incorporated in alum adjuvants were partly protected from clinical disease; the infections that did develop were significantly less severe than those that occurred in control animals injected with adjuvant alone. The results demonstrate that immunization with a purified viral protein can provide significant protection against primary genital infection by HSV-2 in guinea pigs.

Prevention of Type 2 Herpes Simplex Virus Induced Cervical Carcinoma in Mice by Prior Immunization with a Vaccine Prepared from Type 1 Herpes Simplex Virus

M.H. Chen, C.Y. Dong, Z.H. Liu, G.R. Skinner and C.E. Hartley. Vaccine 1983 Dec;1(1):13-6.

Repeated intra-vaginal inoculation of mice with inactivated type 2 herpes simplex virus induced cervical carcinoma in approximately 50 percent of mice. Prior immunization with subunit vaccine Ac NFU1(S-) BHK reduced the frequency of cervical carcinoma to 19 percent. Inoculation of mice with a control preparation of uninfected cell extract never induced preinvasive or invasive cervical cancer. There was evidence of an antibody response in every vaccinated and/or innoculated animal. Mice developing cervical cancer had a significantly higher antibody titre to type 2 herpes virus than mice not developing cancer. These results are in general accord with sero-epidemiological studies of preinvasive and invasive cervical carcinoma in human subjects and suggests that this experimental model may be appropriate for further investigation of prevention of human cervical cancer by vaccination.

Experimental Model for Activation of Genital Herpes Simplex Virus

H. Wrzos and F. Rapp. J Infect Dis 1985 Feb;151(2):349-54.

We have been actively studying herpes virus latency and the effect of antiviral agents on latent infections in vivo and in vitro. To establish a model of recurrent herpetic genital disease, we treated latently infected C57Bl/6 mice with immunosuppressive agents. Mice were injected intraperitoneally with cyclophosphamide and antilymphocyte serum and then were examined for reactivated virus or recurrent lesions. When latently infected mice were subjected to immunosuppression, neither recurrent lesions nor virus was detected at the site of primary infection. However, when mice were selected for immunosuppressive treatment by the presence of postinfection scars, recurrent disease was induced. The results point to the significance of local factors in the pathogenicity of recurrent herpetic genital disease in mice.

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Human Papillomavirus Infection

Clinical

Diffuse Viral Papillomatosis (Condyloma) of the Uterine Cavity

V.S. Venkataseshan and T.H. Woo. Int J Gynecol Pathol 1985;4(4):370-7.

A case of viral papillomatosis (condyloma) of the uterine cervix is reported, which was followed for 13 years and in which the lesion spread to involve superficially the entire uterine cavity without any change in its histologic appearance. The presence of intranuclear papillomavirus antigen was demonstrated by using the peroxidase-antiperoxidase technique.

Genital Condylomas in Immunosuppressed Women: A Therapeutic Challenge

H.B. Krebs, V. Schneider, W.G. Hurt and D.R. Goplerud. South Med J 1986 Feb;79(2):183-7.

Of 30 immunosuppressed women with genital condylomas, 20 (67%) had associated neoplasia of the lower genital tract. We retrospectively studied 11 patients with flat condylomas confined to the cervix; all lesions were eradicated by conventional therapy. Three patients studied retrospectively and 16 studied prospectively had condylomatous lesions involving several sites within the lower genital tract. These lesions were unusually resistant to various treatment methods. Maintenance therapy with 5-fluorouracil (5-FU) cream resulted in a significantly higher control rate (6/7 patients, 86%) than could be achieved otherwise (2/9 patients, 22%; P less than .025). We conclude that ablative therapy by surgery or topical chemical agents followed by maintenance therapy with 5-FU cream may be the treatment of choice for condylomas and other human papillomavirus-associated lesions of the lower genital tract in immunosuppressed women.

Cervical Intraepithelial Neoplasia and Condyloma: An Analysis of Diagnostic Accuracy of Posttreatment Follow-Up Methods

T. Falcone and A. Ferenczy. Am J Obstet Gynecol 1986 Feb;154(2):260-4.

The appropriate follow-up method of patients treated for cervical intraepithelial neoplasia and condyloma is controversial. One school of thought favors cytologic testing alone, whereas the other favors cytologic testing combined with colposcopy. We have analyzed the records of 750 patients treated for cervical intraepithelial neoplasia or condyloma or both in our Colposcopy Clinic. Cytologic testing, colposcopy, and histologic examination were done routinely at 3 to 4, 6 to 8, and 12 to 15 months after treatment of the above conditions in 750 patients. Totals of 95 percent and 5 percent of all 128 persistent lesions were detected by histologic examination at the first (3 to 4 months) and second (6 to 8 months) posttreatment visits, respectively. The combined false negative rates for both visits were 23 percent for cytologic testing, 8 percent for colposcopy, and 5 percent for histologic examination. False negative rates at first visits were 1.5 percent for colposcopy combined with cytologic testing. These observations suggest that colposcopy and, if appropriate, histologic examination significantly contribute to cytologic testing for diagnosing the majority of persistent disease during the first posttreatment visit. Cytologic testing alone seems to be sufficient for the subsequent follow-up of patients treated for cervical intraepithelial neoplasia and/or condyloma.

Human Papillomavirus Types 16 and 18 in Carcinomas of the Penis from Brazil

D.J. McCance, A. Kalache, K. Ashdown, L. Andrade, F. Menezes, P. Smith and R. Doll. Int J Cancer 1986 Jan 15;37(1):55-9.

Human papillomavirus (HPV) type-16 DNA sequences were found in 26/53 (49%) and HPV type-18 in 5/53 (9%) of penile cancers. In only one specimen was HPV18 found on its own. HPV16 sequences were integrated into the host cell chromosomes although some monomeric and oligomeric free forms of DNA were detected in a few tissues. HPV18 was, as far as detectable, free and unintegrated in all tissues tested. HPV16 DNA was also detected in 40 percent of cases of carcinoma of the cervix in 19 women from the same social groups as the males. The viral DNA in the female cases was a mixture of integrated and free forms. The DNA binding protein (ICSP 11/12) of herpes simplex type 2 (HSV2) was not detected in 10 penile cancers tested with a monoclonal antibody.

Association of Human Papillomavirus and *Chlamydia trachomatis* Infections with Incidence Cervical Neoplasia

M.R. Cardillo. Eur J Gynaecol Oncol 1985;6(3):218-21.

Out of a sample of 2,470 smears screened in order to identify cervical intraepithelial neoplasia (CIN), 67 (2.712%) smears were selected. Thirty-nine (58.21%) of these showed evidence of human papillomavirus infection (HPV), 28 (41.79%) showed changes which suggested chlamydial infections (Ct). Results were verified by means of direct immunofluorescence tests (IF) and confronted with colposcopic and cytologic findings. The cytologic findings suggest a possible association between HPV and Ct infections with the incidence of the cervical neoplasia.

Condyloma Acuminata in Children

G. Stringel, S. Mercer and L. Corsini. J Pediatr Surg 1985 Oct;20(5):499-501.

Condyloma acuminata (venereal warts) are sexually transmitted involving the human papillomavirus. It has become commoner in adults in the last decade. While infection is most often by sexual intercourse, it can be transmitted at birth and with close contact with infected individuals. It is common in marked sexual promiscuity. Condyloma acuminata in children should alert the physician to the possibility of sexual abuse or early sexual activity. We report 14 cases of condyloma acuminata in children; from 6 months to 17 years. Sex incidence was equal. All had social and family problems in common, except for one who developed perianal condyloma after repeated rectal dilatations because of a pull through procedure for Hirschsprung's Disease. Two cases of sexual abuse were documented. Treatment methods included podophyllin, liquid nitrogen, 5 fluorouracil cream, fulguration and laser therapy. An adequate social history was available only in six cases. Investigations should include VDRL and cultures for gonococcus, careful medical and social history for neglect or abuse.

Chlamydial Cervicitis in Women Followed-Up for Human Papillomavirus (HPV) Lesions of the Uterine Cervix

K. Syrjanen, R. Mantyjarvi, M. Vayrynen, O. Castren, M. Yliskoski and S. Saarikoski. Acta Obstet Gynecol Scand 1985;64(6):467-71.

To assess the concomitant appearance of *Chlamydia trachomatis* and human papillomavirus (HPV) (currently linked with the development of cervical cancer) in uterine cervix, a series of 250 women under continuous observation for cervical HPV lesions (with or without concomitant cervical intra-epithelial neoplasia (CIN)) were the subject of cervical culturing for *C. trachomatis*, as well as for IP-PAP (indirect immunoperoxidase) staining of the cervical biopsies with monoclonal antibody to *C. trachomatis*. Chlamydia-positive staining was found in only 2/204 biopsies (0.98%), whereas chlamydia could be isolated from the cervix of as many as 26/250 (10.4%) women. In repeat cultures, chlamydia was isolated in 39/936 specimens (4.2%), reflecting the effect of the treatment instituted. The results are discussed in terms of the suggested association of chlamydia with CIN, as well as of the possible synergism between chlamydia and HPV in cervical oncogenesis. The conclusion is drawn that chlamydia and HPV are covariables of sexual behavior, their concomitant appearance in the uterine cervix most probably being ascribable to sexual promiscuity.

Condylomata acuminata in Children: Report of Four Cases

M.A. Sait and B.R. Garg. Genitourin Med 1985 Oct;61(5):338-42.

Four cases of *Condylomata acuminata* in children (two boys, two girls) are reported. Three children had perianal warts and one vulvar warts. One of the four children had been sexually assaulted, but a history of sexual contact was absent in the other three. Surgical excision was undertaken in one case and the others responded well to the local application of 25 percent podophyllin in benzoin tincture compound. In the absence of sexual contact, a non-coital mode of transmission of infection could be a possibility.

The Changing Concepts of Condyloma. A Retrospective Study of Colposcopically Directed Cervical Biopsies

M.A. Binder, G.W. Cates, H.E. Emson, S.J. Valnicek, T.B. MacLachlan, E.W. Schmidt, D.R. Popkin and A. Ferenczy. Am J Obstet Gynecol 1985 Jan 15;151(2):213-9

Human papillomavirus has been implicated in the etiology of cervical intraepithelial neoplasia. A retrospective audit was conducted on all colposcopically directed biopsies performed from June through November, inclusive, in the years 1980 and 1982, a total of 317 cases. In 1980, the misdiagnosis rate for condyloma was 88.9 percent (69 of 78) and, in 1982, the misdiagnosis rate was reduced to 28.5 percent (40 of 140). On review, the association of cervical intraepithelial neoplasia with condyloma was 73 percent (107 of 146), p less than 0.005. The differences in mean ages of patients with condyloma alone, cervical intraepithelial neoplasia with condyloma, and cervical intraepithelial neoplasia alone were significant, p less than 0.02. When condyloma is not recognized, the pathologist tends to overdiagnose grade 3 cervical intraepithelial neoplasia as shown in 28 original cases; 16 of 28 (57.1%) were condyloma alone on review. Fifteen (53.6%) of these 28 patients underwent a cone biopsy or hysterectomy when a less radical procedure would have been acceptable. The morphologic changes indicating cervical condyloma were not fully appreciated by the pathologist, and this resulted in overdiagnosis and later overtreatment by the gynecologist.

Relationship Between Cervical Condylomata, Pregnancy, and Subclinical Papillomavirus Infection

R. Garry and R. Jones. J Reprod Med 1985 May;30(5):393-9.

From a retrospective study of 415 sets of colpophotographs, 25 clinically obvious condylomata of the cervix were identified. Two morphologically distinct forms were found and termed erythrocondylomata and leukocondylomata on the basis of their colposcopic appearance. Erythrocondylomata are red, raised lesions with diagnostic large capillary loops. Those lesions were found in young women (mean age, 22 years) and associated with pregnancy in 72 percent of cases. They were observed to involute and disappear to the naked eye within a few months of the diagnosis. Colposcopic and histologic studies, however, indicated that the lesions could persist in subclinical form. Of eight such lesions studied, five showed histologic and colposcopic features of subclinical papillomavirus infection, and two showed histologic features compatible with cervical intraepithelial neoplasia (CIN). Leukocondylomata are brilliant white lesions associated histologically with a thick layer of keratin over a typical condylomatous base. Those lesions occurred at a later age (mean, 32 years), were not associated with pregnancy, and tended to increase rather than involute with time. Epidemiologic studies have indicated that it is the young and sexually active who are at most risk of developing cervical cancer. This study indicated that it is this same group that is also at highest risk of developing erythrocondylomata of the cervix. Such lesions have been shown to involve the squamocolumnar junction and transformation zone when that area is most active and vulnerable. The progression of such lesions to subclinical papillomavirus infection and CIN suggests that they may be involved in the initiation of the cervical neoplastic process.

Cervical Intraepithelial Neoplasms and Flat Condylomata. Study of 165 Cases (French)

L. Miglianico, M. Reynes and P. Poitout. Ann Pathol 1984 Dec;4(5):325-8.

English summary: Two hundred and five cervical biopsies and diagnostic colonizations performed among 165 women with dysplasias and carcinomas in situ (CIS) were revised with actual concepts of flat condylomata (FC) and cervical intraepithelial neoplasias (CIN). Usual statistical tests were used to analyze the significance of the average age of the different groups (FC alone, FC + CIN, CIN alone) and according to the different grades of CIN. The association between FC and the different grades of CIN was studied with the X2 test. In 66.8 percent of the cases, FC was present, associated or not with CIN. That ends up to be a modification of the diagnosis in 37.6 percent of the cases (reduction of a grade of CIN, substitution of a mild dysplasia CIN I by a FC). In 33.8 percent of the cases, FC was associated with CIN. In this work, the average age between CIN associated with FC was 8 years less than CIN alone. The X2 test applied to the frequency of association between FC and CIN according to the grade of CIN has shown that a statistically valid difference between the grades exists. In the higher grades, the morphological characters of the FC are rare. These observations suggest an integration of the viral genome in the host genome as it has been proved for the shope papilloma and the verruciformis epidermodysplasia.

Electron Microscopic Assessment of Cervical Punch Biopsies in Women Followed-Up for Human Papillomavirus (HPV) Lesions

K. Syrjanen, M. Vayrynen, M. Hippelainen, O. Castren, S. Saarikoski and R. Mantyjarvi. Arch Geschwulstforsch 1985;55(2):131-8.

Cervical punch biopsies from 102 women prospectively followed-up for HPV (Human papillomavirus) lesions (flat, inverted and papillomatous condylomas) were assessed on transmission electron microscopy (TEM) for the presence of HPV particles. The virus discovery rate was correlated with the other characteristics of significance to the clinical behavior (natural history) of these lesions, i.e., the colposcopic pattern, expression of papillomavirus genus specific structural antigens (demonstrated by an indirect immunoperoxidase, IP-PAP technique), as well as the degree of HPV-associated cervical intraepithelial neoplasia (CIN). Virus particles were disclosed with equal frequency in all three types of HPV lesions. Noteworthy, and so far unreported, was the discovery of HPV particles in 56 and 64 percent of the biopsies derived from the epithelium without colposcopic or histological evidence (cytopathic effects) of HPV lesions, respectively. The degree of CIN was without influence on the virus discovery rates. Viral particles were present with equal frequency (57 and 60%, respectively) in the lesions expressing HPV antigens and in those which did not. The highest frequency (89%) of viral particles was found in lesions presented with warty or mosaicism pattern in colposcopy. The implications of these findings to understanding the biology of HPV infections in the uterine cervix is discussed, and the importance of TEM in the follow-up of these lesions is emphasized.

Prevalence of Papillomarvirus Infection in Colposcopically Directed Cervical Biopsy Specimens in 1972 and 1982

S.G. Bernstein, R.L. Voet, D.S. Guzick, J.T. Melancon, L. Ronan-Cowen, S. Lifshitz and H.J. Buchsbaum. Am J Obstet Gynecol 1985 Mar 1;151(5):577-81.

A total of 1,264 consecutive cervical biopsy specimens obtained at the Parkland Memorial Hospital Dysplasia Clinic during 1972 were reviewed. Histopathologic specimens were assessed with special reference to changes induced by human papillomavirus. In 1972, only 0.7 percent of biopsy specimens were reported as consistent with human papillomavirus infection. Upon review, however, 36.5 percent of these specimens were found to demonstrate histologic criteria for the diagnosis of human papillomavirus infection. Approximately half of biopsy specimens reclassified as human papillomavirus were originally interpreted as inflammation; the others were interpreted as cervical intraepithelial neoplasia. Patients with human papillomavirus infection were significantly younger than patients with cervical intraepithelial neoplasia (24.9 versus 30.2 years). These findings were compared with 965 cervical biopsy specimens obtained in 1982. Thirty-four percent of these biopsy specimens revealed human papillomavirus infection. These observations support the concept that human papillomavirus infection of the cervix is not a new entity but a previously unrecognized finding whose prevalence has been relatively stable over a 10-year period.

Laboratory Diagnosis

Detection of Viral DNA and RNA by In Situ Hybridization

J.K. McDougall, D. Myerson and A.M. Beckmann. J Histochem Cytochem 1986 Jan;34(1):33-8.

Using cloned restriction endonuclease fragments of Herpes simplex virus (HSV), human papillomavirus (HPV), and cytomegalovirus (CMV) DNA as probes, viral DNA and RNA sequences have been detected in human tissues. The probes were labeled either with a radioactive isotope, for subsequent detection by autoradiography, or with biotin. This latter technique has been successfully used to visualize HPV DNA in tissues that have been fixed in formalin and embedded in paraffin, and is therefore of value in retrospective studies of histological specimens. HPV DNA was detected under nonstringent conditions (Tm = -42 degrees C) with heterologous probes in plantar and common warts, laryngeal papillomas, and anogenital condylomas. The specific type of HPV was established using stringent hybridization conditions (Tm = −17 degrees C). Results from these and from malignant tissues show the distribution and localization of HSV and HPV RNA and DNA sequences in malignancies of squamous cell origin in the anogenital region. Both HSV and HPV DNA sequences have occasionally been detected in the same tumor, providing a further impetus to test the hypothesis that an initiator-promoter relationship might involve these common human viruses in the development of some tumors.

Therapy

Refractory *Condylomata acuminata:* A Controlled Clinical Trial of Carbon Dioxide Laser Versus Conventional Surgical Treatment

B.R. Duus, T. Philipsen, J.D. Christensen, F. Lundvall and J. Sndergaard. Genitourin Med 1985 Feb;61(1): 59-61.

Uncontrolled trials indicate that treatment of *Condylomata acuminata* with the carbon dioxide laser is effective and probably superior to conventional surgical treatment. We performed a controlled study of refractory *Condylomata acuminata* to clarify whether this is the case. In this randomized trial 21 patients were treated with the carbon dioxide laser and 22 by conventional surgery after having been treated with podophyllin for an average of 33 and 35 weeks, respectively. Five and seven patients, respectively, had previously required additional treatment, such as an operation. The treatment schedule was equally effective for both groups of patients. No difference between the two groups was seen in numbers of recurrences, postoperative pain, healing time, and rate of scar formation (p greater than 0.1—0.2). Treatment of recalcitrant *Condylomata acuminata* with the carbon dioxide laser did not offer any advantages over traditional surgery, including electrocautery.

The Role of the Argon Laser in the Treatment of *Condylomata acuminata* of the Anal Margin and Canal (French)

T. Patrice, B. Dreno, P. Jutel, D. Cloarec, H. Barriere and L. Le Bodic. Ann Gastroenterol Hepatol (Paris) 1985 Oct-Nov;21(5):283-5.

English summary: Condyloma acuminata of the anal margin or anal canal raise therapeutic problems as soon as they become important. In this study, we report the results obtained by 24 patients after Argon-ion laser therapy. This laser, the beam of which is mainly absorbed by hemoglobin, allowed us to cure 91.7 percent of our patients. This result was obtained in one session (14 patients) or two sessions (10 patients) with at least 3 months as follow-up. Furthermore, we notice the excellent quality of cicatrization and the complete lack of incidents during or after the treatment. Argon laser could be a new kind of treatment used preferentially in extensive genital warts.

Human Lymphoblastoid Interferon (Wellferon) in Primary Therapy of Two Children with *Condylomata acuminata*

K.F. Trofatter, Jr., P.C. English, C.E. Hughes and S.A. Gall. Obstet Gynecol 1986 Jan;67(1):137-40.

Human lymphoblastoid interferon (Wellferon) was administered parenterally to two prepubertal girls as primary therapy for genital *Condylomata acuminata*. One child probably had contracted the disease as the result of sexual molestation. Both patients experienced minimal side effects during therapy and underwent complete remission within six weeks. These cases support use of interferon as primary therapy in young patients with extensive condylomata and in those who may have contracted the disease as the result of sexual abuse.

Comparison of Podophyllin Application with Simple Surgical Excision in Clearance and Recurrence of Perianal *Condylomata acuminata*

S.L. Jensen. Lancet 1985 Nov 23;2(8465):1146-8.

Sixty patients with first-episode perianal *Condylomata acuminata* were randomly assigned to podophyllin application or surgical excision. Fifty-eight percent of the male patients were homosexual and 33 percent of the female patients regularly had anal intercourse. Podophyllin completely cleared warts from 23 of 30 (76.6%) patients compared with 28 of 30 (93.3%) for surgical excision. After wart clearance, the cumulative recurrence rates were 18 percent for surgical excision and 43 percent for podophyllin at 3 months (p less than 0.05), 22 percent and 56 percent at 6 months (p less than 0.01), 26 percent and 56 percent at 9 months (p less than 0.01), and 29 percent and 65 percent at 12 months (p less than 0.01). All patients were treated as outpatients and all surgical procedures were carried out under local anesthesia. Both regimens were well tolerated.

Condylomata acuminata in Women: The Effect of Concomitant Genital Infection on Response to Treatment

C. Cooper and H.S. Singha. Acta Derm Venereol (Stockh) 1985;65(2):150-3.

Three hundred and sixteen women with genital warts were studied to relate treatment response to concomitant genital infection at presentation. There was a highly significant difference between the response patterns of those patients who presented with warts alone, and those presenting with other infections (most commonly candidiasis and nonspecific vaginitis). The diagnosis and treatment of associated infections hastens the response of warts to cytotoxic therapy, but there appears to be a subgroup amongst women presenting with warts alone, who require a considerably longer course of treatment. The relevance of these findings to the pathogenesis and management of genital warts is discussed.

Human Fibroblast Interferon in Cervical and Vulvar Intraepithelial Neoplasia Associated with Papilloma Virus Infection

G. De Palo, B. Stefanon, F. Rilke, S. Pilotti and M. Ghione. Int J Tissue React 1984;6(6):523-7.

The follow-up is presented for 13 patients with cervical intraepithelial neoplasia (CIN) grade II-III and vulvar intraepithelial neoplasia (VIN) grade III associated with papilloma virus infection, treated with human fibroblast interferon. Treatment consisted of 2-3 X 10(6) IU interferon per day injected intra- and peri-lesionally for five days per week for 2-3 weeks, with or without a cream topically applied at the dose of 1.2 X 10(6) IU/day X five days. Among the 13 patients with CIN and VIN, 7 complete (54%) and 2 partial regressions were observed. The duration of response appeared to be between 2 and 14 months. Fever, chills, and fatigue were the tolerable side-effects. Our results indicate that treatment with interferon is active against CIN and VIN associated with papilloma virus infection.

Five Years' Use of CO2 Laser in the Treatment of Cervical Lesions: 475 Treated Cases (Mainly Dysplasias and Carcinomas In Situ) (French)

G. Sadoul, T. Beuret and M. Barbagelatta. J Gynecol Obstet Biol Reprod (Paris) 1984;13(6):681-90

English summary: The authors have used the CO2 laser for the treatment of cervical lesions since 1979. Four hundred seventy-five cases were treated, of whom three-quarters were suffering from dysplasia or carcinoma in situ. The cases were discovered by smears from the cervix and vagina and by colposcopy and were confirmed by biopsy. The ways in which the treatment could be conducted depended on the site and not on the severity of the lesion, so long as cases of micro-invasion were excluded. When the lesion was sited on the ectocervix the treatment consisted, after taking a small biopsy for histological checking, in the destruction of the lesion using a laser attached to a microscope. When the lesion was endocervical, conization had to be carried out using a laser attached to an apparatus held in the hand. Colposcopic examination carried out 15 to 20 days after treatment made it possible to discover whether the treatment had been complete or not. Recurrences are characterized by the return of colposcopic and cytological abnormalities. Sometimes these are only cytological and may occur 6 to 18 months after treatment. After 5 years the level of recurrences is remarkably low and is less than 4 percent. Secondary complications such as hemorrhage are very rare, and the morphology of the cervix is hardly changed except in a few cases. The operator must know very well indeed how to use the colposcope to undertake such treatments successfully.

Research and Evaluation

Male Influences on Cervical Cancer Risk

M.V. Zunzunegui, M.C. King, C.F. Coria and J. Charlet. Am J Epidemiol 1986 Feb;123(2):302-7.

Risk factors for squamous cell carcinoma of the uterine cervix were studied among low income, married Hispanic women and their husbands, using a case-control design. A total of 45 eligible cases were identified at public hospitals and community clinics in the San Francisco Bay Area. For each case, a control was selected within two years of age from among Hispanic women seen at the same institution. Thirty-nine matched pairs of couples were interviewed to assess histories of sexual behavior and other possible risk factors. Cases and controls differed markedly in the number of past sexual partners of their husbands. Cases were 5.3 times more likely to be married to husbands who had had 20 or more sexual partners than were controls. Cases and controls themselves did not differ in their number of sexual partners, but cases were younger at first intercourse than were controls. The association with husband's sexual history persisted after adjusting for the woman's number of sexual partners or age at first intercourse. These results support the infectious and venereal transmission of cervical cancer and indicate the important role of husbands in its occurrence in a population with high incidence rates.

Morphological Transformation In Vivo of Human Uterine Cervix with Papillomavirus from *Condylomata acuminata*

J.W. Kreider, M.K. Howett, S.A. Wolfe, G.L. Bartlett, R.J. Zaino, T. Sedlacek and R. Mortel. Nature 1985 Oct 17-23;317(6038):639-41.

Carcinoma of the human uterine cervix has been associated with several infectious agents including papillomavirus. Papillomavirus group-specific antigen (GSA) and viral particles have been demonstrated in human *Condylomata acuminata* (CA) and flat warts of the uterine cervix. Cell alterations consisting of nuclear enlargement, hyperchromasia, irregularity, binucleation and cytoplasmic clearing (koilocytosis) are often interpreted as mild to moderate dysplasia. Present evidence that human papillomavirus (HPV) is responsible for the development of these lesions relies on the association of GSA and virus particles in the affected tissue, fulfilling the first two of Koch's postulates. Direct proof of an etiological relationship, however, requires induction of the CA change in normal, human uterine cervix after exposure to papillomavirus. Infecting human subjects with HPV is ethically unacceptable and no satisfactory alternative systems have been defined. Also, human cell cultures do not support growth or transformation by HPV. Here we report the first demonstration of the morphological transformation of human tissues with a human papillomavirus under controlled, experimental conditions. 'Transformation' is used here in its literal sense to refer to a heritable morphological alteration in the appearance of the cells. The use of this term does not indicate that the changes described are neoplastic, but they are identical to the dysplastic changes found in biopsies of uterine cervical CA. Our results demonstrate the direct involvement of CA virus in dysplastic change of human cervical tissue and indicate that the experimental system described may be useful in elucidating the contribution of human papillomaviruses to the pathogenesis of human cervical cancer.

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Acquired Immunodeficiency Syndrome

Clinical

Cryptococcal Disease in Patients with the Acquired Immunodeficiency Syndrome. Diagnostic Features and Outcome of Treatment

A. Zuger, E. Louie, R.S. Holzman, M.S. Simberkoff and J.J. Rahal. Ann Intern Med 1986 Feb;104(2):234-40.

Between January 1, 1981 and December 1, 1984, 34 of 396 patients with the acquired immunodeficiency syndrome (AIDS) developed cryptococcal infections. Twenty-six cases are reviewed. Twenty-two patients had brain or meningeal disease; the others had pulmonary disease (2 patients), pericarditis (1 patient), and antigenemia (1 patient). During treatment, three patients died of cryptococcosis and three died of other causes. Fifteen patients were followed for more than 6 weeks after treatment. Of eight patients who received no additional amphotericin B, four had relapses and died of cryptococcosis within 6 months, three died of other causes, and one survived. Of seven patients who received maintenance therapy with amphotericin B, none had relapses, three died of other causes, and four survived. Our data suggest that maintenance therapy with amphotericin may be needed to prevent relapse in patients with AIDS.

Demonstration of Antibodies to Human T-Lymphotropic Retrovirus Type III in Lymphoadenopathy Syndrome Patients and in Individuals at Risk for Acquired Immune Deficiency Syndrome (AIDS) in Italy

M.C. Sirianni, P. Rossi, M. Moroni, S. Romagnani, A. Lazzarin, M. Carbonari, B. Scarpati, M. Mariani, P.E. Manconi, G.S. Del Giacco, et al. Am J Epidemiol 1986 Feb;123(2):308-15.

An epidemiologic survey of the distribution of lymphoadenopathy syndrome in six Italian cities and its correlation with human T-lymphotropic retrovirus III (HTLV-III) is reported. Serum samples of nine patients with acquired immune deficiency syndrome (AIDS) were tested, 180 from patients with lymphoadenopathy and 349 from individuals belonging to groups such as homosexuals, drug addicts, hemophiliacs, and polytransfused considered at increased risk for AIDS. Prevalence of HTLV-III antibodies was 78 percent in AIDS patients and 61 percent in 180 patients with lymphoadenopathy syndrome (variation among drug abusers by city from 51% in Cagliari to 87% in Rome). The percentage of positive sera in individuals at risk for AIDS or lymphoadenopathy ranged from 0 percent in polytransfused to 8.5 percent in homosexuals, 14 percent in drug addicts, and 19.5 percent in hemophiliacs. No positive sera were found among 660 healthy individuals including relatives of patients with AIDS or lymphoadenopathy or in 342 patients suffering from immunologic or infectious diseases. These results strongly suggest that HTLV-III is the causative agent of AIDS and lymphoadenopathy. Since none of the healthy subjects were positive while a substantial percentage of people at risk for AIDS showed antibodies to HTLV-III, it may be presumed that this infection is also prevalent in the Italian population group in which AIDS and lymphoadenopathy are most likely to develop.

Three-Year Incidence of AIDS in Five Cohorts of HTLV-III-Infected Risk Group Members

J.J. Goedert, R.J. Biggar, S.H. Weiss, M.E. Eyster, M. Melbye, S. Wilson, H.M. Ginzburg, R.J. Grossman, R.A. DiGioia, W.C. Sanchez, et al. Science 1986 Feb 28;231(4741):992-5.

The incidence of the acquired immune deficiency syndrome (AIDS) among persons infected with human T-lymphotropic virus type III (HTLV-III) was evaluated prospectively among 725 persons who were at high risk of AIDS and had enrolled before October 1982 in cohort studies of homosexual men, parenteral drug users, and hemophiliacs. A total of 276 (38.1%) of the subjects were either HTLV-III seropositive at enrollment or developed HTLV-III antibodies subsequently. AIDS had developed in 28 (10.1%) of the seropositive subjects before August 1985. By actuarial survival calculations, the 3-year incidence of AIDS among all HTLV-III seropositive subjects was 34.2 percent in the cohort of homosexual men in Manhattan, New York, and 14.9 percent (range 8.0 to 17.2%) in the four other cohorts. Out of 117 subjects followed for a mean of 31 months after documented seroconversion, five (all hemophiliacs) developed AIDS 28 to 62 months after the estimated date of seroconversion, supporting the hypothesis that there is a long latency between acquisition of viral infection and the development of clinical AIDS. This long latency could account for the significantly higher AIDS incidence in the New York cohort compared with other cohorts if the virus entered the New York homosexual population before it entered the populations from which the other cohorts were drawn. However, risk of AIDS development in different populations may also depend on the presence of as yet unidentified cofactors.

AIDS Virus Infection in Nairobi Prostitutes. Spread of the Epidemic to East Africa

J.K. Kreiss, D. Koech, F.A. Plummer, K.K. Holmes, M. Lightfoote, P. Piot, A.R. Ronald, J.O. Ndinya-Achola, L.J. D'Costa, P. Roberts, et al. N Engl J Med 1986 Feb 13;314(7):414-8.

The acquired immunodeficiency syndrome (AIDS) is epidemic in Central Africa. To determine the prevalence of AIDS virus infection in East Africa, we studied 90 female prostitutes, 40 men treated at a clinic for sexually transmitted diseases, and 42 medical personnel in Nairobi, Kenya. Antibody to human T-cell lymphotropic virus Type III (HTLV-III) was detected in the serum of 66 percent of prostitutes of low socioeconomic status, 31 percent of prostitutes of higher socioeconomic status, 8 percent of the clinic patients, and 2 percent of the medical personnel. The presence of the antibody was associated with both immunologic and clinical abnormalities. The mean T-cell helper/suppressor ratio was 0.92 in seropositive prostitutes and 1.82 in seronegative prostitutes (P less than 0.0001). Generalized lymphadenopathy was present in 54 percent of seropositive prostitutes and 10 percent of seronegative prostitutes (P less than 0.0001). No constitutional symptoms, opportunistic infections, or cases of Kaposi's sarcoma were present. Our results indicate that the epidemic of AIDS virus infection has, unfortunately, spread extensively among urban prostitutes in Nairobi, Kenya. Sexual exposure to men from Central Africa was significantly associated with HTLV-III antibody among prostitutes, suggesting transcontinental spread of the epidemic.

Lack of Transmission of HTLV-III/LAV Infection to Household Contacts of Patients with AIDS or AIDS-Related Complex with Oral Candidiasis

G.H. Friedland, B.R. Saltzman, M.F. Rogers, P.A. Kahl, M.L. Lesser, M.M. Mayers and R.S. Klein. N Engl J Med 1986 Feb 6;314(6):344-9.

To determine the risk of transmission of human T-cell lymphotropic virus Type III/lymphadenopathy-associated virus (HTLV-III/LAV) to close but nonsexual contacts of patients with the acquired immunodeficiency syndrome (AIDS), we studied the nonsexual household contacts of patients with AIDS or the AIDS-related complex with oral candidiasis. Detailed interviews, physical examinations, and tests for serum antibody to HTLV-III/LAV were performed on 101 household contacts of 39 AIDS patients (68 children and 33 adults), all of whom had lived in the same household with an index patient for at least three months. These contacts had shared household items and facilities and had close personal interaction with the patient for a median of 22 months (range, 3 to 48) during the period of presumed infectivity. Only one of 101 household contacts—a five-year-old child—had evidence of infection with the virus, which had probably been acquired perinatally rather than through horizontal transmission. This study indicates that household contacts who are not sexual partners of, or born to, patients with AIDS are at minimal or no risk of infection with HTLV-III/LAV.

Risk Factors Associated with AIDS in Haiti

J.W. Pape, B. Liautaud, F. Thomas, J.R. Mathurin, M.M. St. Amand, M. Boncy, V. Pean, M. Pamphile, A.C. Laroche and W.D. Johnson, Jr. Am J Med Sci 1986 Jan;291(1):4-7.

A total of 121 acquired immunodeficiency syndrome (AIDS) patients diagnosed in Haiti were studied between June 1979 and December 1983. Risk factors were identified in 65 percent of 34 patients evaluated in a standardized manner since July 1983 and included: bisexuality, 38 percent; blood transfusion, 21 percent; and intravenous drug abuse or a spouse with AIDS, 6 percent. These risk factors were reported by only 20 percent of the 85 patients studied between June 1979 and June 1983. AIDS patients also reported more frequent parenteral injections prior to the onset of their illness than control subjects (e.g., siblings, friends, sexual partners). Heterosexual activity among female AIDS patients was also greater than in their female controls. It was concluded that, in contrast to the experience reported among Haitians with AIDS in the USA, risk factors are present among most patients with AIDS in Haiti.

A Papular Eruption Associated with Human T Cell Lymphotropic Virus Type III Disease

W.D. James, R.R. Redfield, G.P. Lupton, M.S. Meltzer, T.G. Berger, O.G. Rodman, P.D. Markham, M.G. Sarngadharan, S.Z. Salahuddin and R.C. Gallo. J Am Acad Dermatol 1985 Oct;13(4):563-6.

The clinical spectrum of human T cell lymphotropic virus type III (HTLV-III) disease is associated with myriad cutaneous findings, commonly of infectious origin. A clinically characteristic, yet histologically nonspecific, papular eruption was observed in seven of thirty-five patients followed up for HTLV-III disease (acquired immunodeficiency syndrome and the related complex). Noncoalescing 2- to 5-mm skin-colored papules of the head, neck, and upper trunk typify the lesions. Histologically, a chronic perivascular infiltrate of mononuclear cells was regularly present. The eruption was often, but not always, pruritic. The clinical course was chronic. Many patients had persistent lesions for more than 9 months; however, the number of papules tended to wax and wane with time. Although the cause of this eruption is unknown, it is sufficiently distinct and frequent to be recognized by clinicians as a cutaneous sign of human retrovirus infection.

Antibodies to Human T-Lymphotropic Virus Type III and Development of the Acquired Immunodeficiency Syndrome in Homosexual Men Presenting with Immune Thrombocytopenia

D.I. Abrams, D.D. Kiprov, J.J. Goedert, M.G. Sarngadharan, R.C. Gallo and P.A. Volberding. Ann Intern Med 1986 Jan;104(1):47-50.

In 35 homosexual men with isolated thrombocytopenia at initial presentation, who were evaluated and treated between 1982 and 1984, hematologic studies showed immune destruction. In contrast to findings in other autoimmune conditions, T-lymphocyte subsets in these patients were reversed, with a mean helper to suppressor ratio of 0.4 and with an absolute depletion of helper cells to 390/mm3. An enzyme-linked immunosorbent assay detected antibodies to human T-lymphotropic virus type III in 21 of 25 patients tested; Western blot analysis confirmed seropositivity in the other four patients, who had borderline findings. Although 19 of 24 patients treated with steroids responded, only two achieved sustained normal platelet counts. Ten of fifteen patients who had splenectomy achieved remissions. Three patients treated with steroids or splenectomy developed diagnoses compatible with the acquired immunodeficiency syndrome 16 to 34 months after their initial presentation with thrombocytopenia. These findings indicate that immune thrombocytopenia is part of the clinical spectrum of the acquired immunodeficiency syndrome.

Reported Changes in the Sexual Behavior of Men at Risk for AIDS, San Francisco, 1982-84—The AIDS Behavioral Research Project

L. McKusick, J.A. Wiley, T.J. Coates, R. Stall, G. Saika, S. Morin, K. Charles, W. Horstman and M.A. Conant. Public Health Rep 1985 Nov-Dec;100(6):622-9.

We surveyed 454 men in November 1983 and in May 1984 regarding their sexual practices during the month before the survey. In the 1983 survey, we also asked for reports about sexual behavior during the same month 1 year prior to the survey. The sample consisted of men recruited as they left bath-houses and bars, men who had not used bars or baths for meeting sexual partners for 2 months prior to the November 1983 survey, and men in committed primary relationships with another man. We found substantial changes in reported sexual behavior with persons other than a primary partner. The average number of male partners declined from 6.3 in November 1982 to 3.9 in May 1984. Receptive anal intercourse without condom declined from 1.9 to 0.7, oral-anal contact declined from 1.1 to 0.3, and swallowing semen declined from 2.8 to 0.7 in terms of the number of times that the respondent engaged in the act in the last month. These same changes did not occur in relation to sex with a primary partner. Only one variable, increased length of time since the first homosexual experience, distinguished persons maintaining few sexual partners from those increasing the number of sexual partners from November 1983 to May 1984. Four variables distinguished those retaining high numbers of sexual partners from those lowering the number of sexual partners, namely, ability to remember a visual image of AIDS deterioration, age, relationship status, and length of time since first homosexual experience.

Patients at Risk for AIDS-Related Opportunistic Infections. Clinical Manifestations and Impaired Gamma Interferon Production

H.W. Murray, J.K. Hillman, B.Y. Rubin, C.D. Kelly, J.L. Jacobs, L.W. Tyler, D.M. Donelly, S.M. Carriero, J.H. Godbold and R.B. Roberts. N Engl J Med 1985 Dec 12:313(24):1504-10.

We studied 81 men (79 homosexuals and 2 drug abusers) with persistent lymphadenopathy to determine whether those at risk for AIDS-related opportunistic infections could be identified prospectively. (Sixty-nine of 76 (91%) had antibodies to human T-cell lymphotropic virus Type III (HTLV-III), and 76 of 79 (96%) had abnormal T4/T8 cell ratios.) During the follow-up period (mean +/− S.E.M., 12.9 +/− 0.5 months; range, 8 to 19), infections developed in none of 38 patients with lymphadenopathy alone and in only one of 15 (7%) with antecedent herpes zoster infection; however, 13 of 28 (46%) with lymphadenopathy accompanied by constitutional symptoms, or oral candidiasis or both, had opportunistic infections within the follow-up period. Among the results of various T-cell assays, only antigen-stimulated lymphocyte proliferation and gamma interferon generation, which were absent or barely measurable in those in whom AIDS ultimately developed, were of prognostic value. T cells from 15 patients, 11 of whom had constitutional symptoms or thrush, failed to generate antigen-induced gamma interferon; infections developed in 10 of these 15 (67%) within a mean of 8.2 months. These results suggest that patients with AIDS-related complex who are at risk for opportunistic infections within a year can be identified by correlating clinical manifestations with antigen-stimulated T-cell responses—in particular, with the production of gamma interferon.

Isolation of HTLV-III from Cerebrospinal Fluid and Neural Tissues of Patients with Neurologic Syndromes Related to the Acquired Immunodeficiency Syndrome

D.D. Ho, T.R. Rota, R.T. Schooley, J.C. Kaplan, J.D. Allan, J.E. Groopman, L. Resnick, D. Felsenstein, C.A. Andrews and M.S. Hirsch. N Engl J Med 1985 Dec 12;313(24):1493-7.

We conducted virus-isolation studies on 56 specimens from the nervous system of 45 patients in order to determine whether human T-cell lymphotropic virus type III (HTLV-III) is directly involved in the pathogenesis of the neurologic disorders frequently encountered in the acquired immunodeficiency syndrome (AIDS) and the AIDS-related complex. We recovered HTLV-III from at least one specimen from 24 of 33 patients with AIDS-related neurologic syndromes. In one patient, HTLV-III was isolated from the cerebrospinal fluid during acute aseptic meningitis associated with HTLV-III seroconversion. HTLV-III was also isolated from cerebrospinal fluid from six of seven patients with AIDS or its related complex and unexplained chronic meningitis. In addition, of 16 patients with AIDS-related dementia, 10 had positive cultures for HTLV-III in cerebrospinal fluid, brain tissue, or both. Furthermore, we cultured HTLV-III from the spinal cord of a patient with myelopathy and from the sural nerve of a patient with peripheral neuropathy. These findings suggest that HTLV-III is neurotropic, is capable of causing acute meningitis, is responsible for AIDS-related chronic meningitis and dementia, and may be the cause of the spinal-cord degeneration and peripheral neuropathy in AIDS and AIDS-related complex.

Serum Interferon and Clinical Manifestations of Infection with Human T-Lymphotropic Virus Type III

J. Abb. Med Microbiol Immunol (Berl) 1985; 174(4):205-10.

Sera from 32 homosexual men were studied for the presence of antibodies against human T-lymphotropic virus type III (HTLV III) and acid-labile interferon (IFN) alpha. Infection with HTLV III was found to be associated with the presence of serum IFN. IFN was detected in 74 percent of sera from male homosexuals with HTLV III antibody, but in only 6 percent of sera from antibody-negative individuals. More than 80 percent of sera from HTLV III-infected patients with the acquired immune deficiency syndrome (AIDS) or pre-AIDS conditions (generalized lymphadenopathy or the AIDS-related complex) were positive for IFN, while IFN was not present in sera from healthy homosexual men with HTLV III antibody. In conclusion, the presence of serum IFN may be predictive of the development of AIDS or pre-AIDS conditions in male homosexuals exposed to HTLV III.

Kaposi's Sarcoma in Los Angeles, California

R.K. Ross, J.T. Casagrande, R.L. Dworsky, A. Levine and T. Mack. JNCI 1985 Dec;75(6):1011-5.

The demographic characteristics of "classic" Kaposi's sarcoma (KS) and of "epidemic" KS in Los Angeles, CA, were compared with the use of data from the Cancer Surveillance Program, the population-based tumor registry in Los Angeles County. The data obtained document the magnitude of the excess risk of classic KS for Jewish men of European (especially Eastern and Southern European) origin. The data also show, in a systematic way, the magnitude of the increase in acquired immune deficiency syndrome-related KS in one large urban area of the United States. In addition, they demonstrate that the demographic risk factors of religion and birthplace for classic KS are unrelated to epidemic KS and that the clinical presentation in terms of stage and primary site of classic KS is distinct from that of the epidemic form of the disease.

Primary Human T-Lymphotropic Virus Type III Infection

D.D. Ho, M.G. Sarngadharan, L. Resnick, F. Dimarzoveronese, T.R. Rota and M.S. Hirsch. Ann Intern Med 1985 Dec;103(6 (Pt 1)):880-3.

Primary infection with the human T-lymphotropic virus type III (HTLV-III) was documented in three patients by virus isolation during acute illness and concurrent or subsequent HTLV-III seroconversion. All patients had fevers, rigors, arthralgias, and myalgias. Additional symptoms included truncal maculopapular rash, urticaria, abdominal cramps, and diarrhea. Lymphocytic meningitis accompanied the febrile illness in two patients. The estimated incubation period was 4 to 6 weeks, and the symptoms lasted 2 to 3 weeks. Seroconversion occurred 8 to 12 weeks after presumed exposure and was manifested by a characteristic antibody response pattern. Physicians should consider the possibility of primary HTLV-III infection when evaluating patients who belong to one of the risk groups for the acquired immunodeficiency syndrome and who have prolonged febrile illnesses.

Transfusion-Associated Acquired Immunodeficiency Syndrome in the United States

T.A. Peterman, H.W. Jaffe, P.M. Feorino, J.P. Getchell, D.T. Warfield, H.W. Haverkos, R.L. Stoneburner and J.W. Curran. JAMA 1985 Nov 22-29;254(20):2913-7.

By August 15, 1985, one hundred ninety-four cases of possible transfusion-associated acquired immunodeficiency syndrome (AIDS) had been reported to the Centers for Disease Control. Cases received their transfusions in 30 states. Infants account for 10 percent of the cases, suggesting an increased susceptibility to developing AIDS. Investigations one to six years after the transfusions have identified high-risk donors to 47 cases. Of 47 high-risk donors tested, 40 had a reactive serology for human T-cell lymphotropic virus type III/lymphadenopathy-associated virus (HTLV-III/LAV) antibody, including five with no risk for AIDS by history. The HTLV-III/LAV was isolated from 23 of 26 seroreactive high-risk donors, most of whom remained asymptomatic. Blood components that transmitted HTLV-III/LAV included red cells, platelets, plasma, and whole blood. The time from transfusion to diagnosis of AIDS ranged from four to 84 months. The risk of developing AIDS after a blood transfusion has been low and will be lowered further by using both self-deferral and antibody screening.

Seroepidemiological Studies of HTLV-III Antibody Prevalence among Selected Groups of Heterosexual Africans

N. Clumeck, M. Robert-Guroff, P. Van de Perre, A. Jennings, J. Sibomana, P. Demol, S. Cran and R.C. Gallo. JAMA 1985 Nov 8;254(18):2599-602.

T-lymphocyte subsets and human T-cell lymphotropic virus type III antibody prevalence were studied in African patients with the acquired immunodeficiency syndrome (AIDS) or AIDS-related complex (ARC), and in female prostitutes. African blood donors and healthy Zairian and Rwandese persons matched for age, sex, and annual income served as controls. Seropositivity was noted in 46 (87%) of 53 patients with AIDS, 29 (88%) of 33 patients with ARC, 67 (80%) of 84 prostitutes, and five (12.5%) of 40 and eight (15.5%) of 51 healthy controls and blood donors, respectively. Patients with AIDS and ARC had a significantly lower OKT4/OKT8 ratio than healthy African controls. These studies suggest that human T-cell lymphotropic virus type III infection has already spread extensively into the general African population and that female prostitutes could be an important human reservoir of AIDS virus in the heterosexual population.

Lymphomas in Men at High Risk for Acquired Immune Deficiency Syndrome (AIDS)
A Study of 21 Cases

H.L. Ioachim, M.C. Cooper and G.C. Hellman. Cancer 1985 Dec 15;56(12):2831-42

An increased incidence of lymphoid neoplasias is associated with the states of immune deficiency, both congenital and acquired. Twenty-one cases of lymphoma in men at high risk for acquired immune deficiency syndrome (AIDS) were diagnosed in one community hospital in New York City within the last 2 years. The mean age of these patients was 39.6 years, 20 were homosexual, and one was an intravenous drug abuser. There were three Hodgkin's and 18 non-Hodgkin's lymphomas of various histologic types, but almost all of high-grade categories. The proportion of extranodal lymphomas, the involvement of the gastrointestinal tract, central nervous system, bone marrow, and myocardium were significantly higher than in the lymphomas of the general population. The phenotypes were B-cell and non-B-non-T-cell types without any T-cell lymphomas. All patients had reversed helper-suppressor T-cell ratios and all those tested had circulating HTLV-III antibodies. Seven patients have had previous lymph node biopsies performed, showing the lesions of AIDS-related lymphadenopathies that often were directly associated with lymphoma. A variety of severe opportunistic infections and Kaposi's sarcoma affected these patients. All lymphomas in this group were highly aggressive, involved multiple organs, and responded poorly to treatment, resulting in early deaths.

Ethical Dilemmas in Caring for Patients with the Acquired Immunodeficiency Syndrome

R. Steinbrook, B. Lo, J. Tirpack, J.W. Dilley and P.A. Volberding. Ann Intern Med 1985 Nov;103(5):787-90.

Caring for patients with the acquired immunodeficiency syndrome (AIDS) raises ethical dilemmas about when to provide life-sustaining treatments such as mechanical ventilation and cardiopulmonary resuscitation. In addition, many patients become mentally incompetent and unable to participate in decisions. Homosexual men may want their lover or a friend to make decisions for them, but the patient's partner or friend cannot make these decisions unless he is legally designated. Decision-making guidelines may be hard to implement because caring for patients with AIDS is stressful. We describe three cases that illustrate the difficult ethical dilemmas and stresses of caring for these patients.

Implications of the Acquired Immunodeficiency Syndrome for Health Policy

E.N. Brandt, Jr. Ann Intern Med 1985 Nov;103 (5):771-3.

The acquired immunodeficiency syndrome (AIDS) has spread rapidly through the high-risk population and has created fear and anxiety. The health policy implications of such a disorder are difficult to assess because the disease was totally unknown until a few years ago and because it occurs primarily in homosexual men and intravenous drug users. The latter factor has raised sociopolitical issues not present in other epidemics. Detection and surveillance systems, capabilities for prompt and effective scientific response, central coordination of scientific efforts, public information mechanisms, role definitions, and guidelines for funding are needed. The scientific community must study this epidemic and the total societal response to it with a view towards being better prepared in the future.

Social Consequences of the Acquired Immunodeficiency Syndrome

B.J. Cassens. Ann Intern Med 1985 Nov;103(5):768-71.

Awareness of the pertinent psychosocial dimensions of the acquired immunodeficiency syndrome (AIDS) provides researchers and clinicians with an understanding of factors impinging on their relationships with persons at risk for this disease. These observations are made from the standpoint of the American Association of Physicians for Human Rights, a national organization of gay physicians that serves as an advocate in improving health care for gay men and lesbians. Fear and uncertainty in patient care and prognosis as well as loss of confidentiality are among the stresses on gay men with AIDS. Injudicious "expert" pronouncements and sensational stories in the media heighten the fear of persons at risk for the disease as well as the fear and prejudice of the general community. Members of all communities, both heterosexual and gay, scientific and lay, should work together to eliminate social ignorance about AIDS.

Psychosocial Reactions of Persons with the Acquired Immunodeficiency Syndrome

S.E. Nichols. Ann Intern Med 1985 Nov;103(5):765-7.

The psychosocial impact of the acquired immunodeficiency syndrome (AIDS) on patients follows the situational distress model of crisis, transitional state, and deficiency state. Repeated crises in AIDS modify this reaction, and patients may experience a final adjustment, the preparation for death. Additional psychosocial problems are caused by the intensified prejudice against homosexual men and drug addicts. Society itself has been disrupted by the new information about sexual behavior that has been brought to light by AIDS, indicating that primitive sexual taboos still influence modern society. Understanding the various psychosocial reactions to AIDS offers opportunities for social progress and personal growth.

The Psychosocial and Neuropsychiatric Sequelae of the Acquired Immunodeficiency Syndrome and Related Disorders

J.C. Holland and S. Tross. Ann Intern Med 1985 Nov;103(5):760-4.

The acquired immunodeficiency syndrome (AIDS) and its related conditions are a public health problem of unprecedented proportions due to the debilitating and fatal nature of the disease, the sociocultural implications related to contagion, and its initial appearance in certain socially stigmatized groups. The ability of patients to tolerate the consequences of the disease depends on their psychological ability to cope based on emotional strength and the availability of social support. The psychological and social impact of AIDS may result in psychiatric symptoms similar to those seen in other life-threatening diseases, including anxiety, depression, and delirium. Neurologic complications are frequent, the most common being an encephalopathy and dementia that is poorly understood. It is difficult in the early stages of AIDS to separate reactive depression and psychomotor retardation from symptoms associated with central nervous system complications. Guidelines are needed to manage the psychological problems posed by AIDS and its related conditions.

The Acquired Immunodeficiency Syndrome in Haiti

J.W. Pape, B. Liautaud, F. Thomas, J.R. Mathurin, M.M. St. Amand, M. Boncy, V. Pean, M. Pamphile, A.C. Laroche, J. Dehovitz, et al. Ann Intern Med 1985 Nov;103(5):674-8.

Two hundred twenty-nine patients in Haiti with the acquired immunodeficiency syndrome were studied between 1979 and 1984. The clinical spectrum of the syndrome in Haitians was similar in most aspects to that in patients with the disease in the United States. However, in contrast to findings in the United States, accepted risk factors (bisexuality, blood transfusions, intravenous drug abuse) were identified in only 43 percent of Haitian patients. Patients in Haiti with and without these risk factors were similar to each other but differed from age- and sex-matched siblings and friends in the number of heterosexual contacts and receipt of intramuscular injections. These latter activities were more common in patients than in their siblings and friends, and represent potential modes of transmission of infection with the human T-lymphotropic virus type III.

The International Occurrence of the Acquired Immunodeficiency Syndrome

J.B. Brunet and R.A. Ancelle. Ann Intern Med 1985 Nov;103(5):670-4.

Through December 1984, 9,932 cases of the acquired immunodeficiency syndrome have been reported, mainly from North and South America and Europe; 85 percent of these cases occurred in the United States. Haiti and the United States have the highest incidence rates, 59 and 36 per million population, respectively. Rates in the United States range from 0.3 (beginning of 1981) to 10.4 (end of 1984). Brazil, Canada, Denmark, Switzerland, France, West Germany, the United Kingdom, and the Netherlands show a slower increase. Homosexual men and intravenous drug users are still the main risk groups in the United States and Europe. The disease is prevalent in heterosexual Haitians and Africans whether they live in their own countries or abroad. Cases of the syndrome have been identified in Zaire, Rwanda, Zambia, and Uganda, but its full extent is not yet known. Consistent with the general history of epidemics, the appearance of geographically separated sites of incidence of the syndrome could be linked to population migrations; however, no evidence has been found to identify an index location.

The Acquired Immunodeficiency Syndrome in Gay Men

H.W. Jaffe, A.M. Hardy, W.M. Morgan and W.W. Darrow. Ann Intern Med 1985 Nov;103(5):662-4.

The acquired immunodeficiency syndrome (AIDS) is a major health problem for gay men in the United States. About three-fourths of all reported cases have occurred in this population, and the number is projected to double in the next year. In Manhattan and San Francisco, AIDS is now the leading cause of premature mortality in men aged 25 to 44 years who have never married. In a sample of a cohort of gay men enrolled in a San Francisco clinic, 2.7 percent of the men had the syndrome and 26 percent had related conditions in 1984. Antibody to human T-lymphotropic virus, type III/lymphadenopathy-associated virus was found in sera from 67 percent of the men, including 58 percent of asymptomatic men. Behavioral factors associated with an increased risk of AIDS include large numbers of sexual partners, receptive anal intercourse, and "fisting." The adoption of safer lifestyles is currently the basis of attempts to control the syndrome in gay men.

The Epidemiology and Prevention of the Acquired Immunodeficiency Syndrome

J.W. Curran. Ann Intern Med 1985 Nov;103(5):657-62.

The incidence of the acquired immunodeficiency syndrome (AIDS) has continued to increase worldwide. From June 1981 to September 1985, 12,932 cases have been diagnosed and reported in the United States; this number is expected to double during the next year. The incubation period is long and few persons infected with human T-lymphotropic virus type III/lymphadenopathy-associated virus (HTLV-III/LAV) have AIDS diagnosed within 2 to 5 years of infection. The widespread use of HTLV-III/LAV serologic tests to screen donated blood and plasma, the continued deferral of donors from groups with an increased incidence of AIDS, and the use of heat-treated clotting factor concentrates should help prevent HTLV-III/LAV transmission through blood and blood products. Preventing transmission among sexual partners, among intravenous drug users, and from infected mothers to newborns will continue to be difficult without a vaccine, specific antiviral therapy, or both. Risk reduction strategies should involve community groups to provide accurate information and influence behaviors that lead to transmission of the virus.

Evidence against Transmission of Human T-Lymphotropic Virus/Lymphadenopathy-Associated Virus (HTLV-III/LAV) in Families of Children with the Acquired Immunodeficiency Syndrome

J.E. Kaplan, J.M. Oleske, J.P. Getchell, V.S. Kalyanaraman, A.B. Minnefor, M. Zabala-Ablan, V. Joshi, T. Denny, C.D. Cabradilla, M.F. Rogers, et al. Pediatr Infect Dis 1985 Sep-Oct;4(5):468-71.

Six children with the acquired immunodeficiency syndrome (AIDS) and 12 of their household contacts were investigated serologically for evidence of infection with human T-lymphotropic virus/lymphadenopathy-associated virus (HTLV-III/LAV), the presumed etiologic agent of AIDS. All six children had antibody against HTLV-III/LAV, as measured by enzyme-linked immunosorbent assay, in each specimen tested. Of the two mothers studied, both were seropositive; one was diagnosed with and died from AIDS. Four of the remaining 10 household members were seropositive, including three adults in groups at high risk for the development of AIDS and one sibling who was younger than the child with AIDS. Among the seronegative household contacts were four foster mothers or grandmothers of the children with AIDS, three of whom had cared for the children since infancy. Household contact with children with AIDS may include persons in groups at high risk for AIDS who have been infected with HTLV-III/LAV. However, the negative findings in household contacts without risk factors for AIDS suggest that horizontal transmission of the virus within households by means other than sexual contact must be infrequent.

Slim Disease: A New Disease in Uganda and Its Association with HTLV-III Infection

D. Serwadda, R.D. Mugerwa, N.K. Sewankambo, A. Lwegaba, J.W. Carswell, G.B. Kirya, A.C. Bayley, R.G. Downing, R.S. Tedder, S.A. Clayden, et al. Lancet 1985 Oct 19;2(8460):849-52.

A new disease has recently been recognized in rural Uganda. Because the major symptoms are weight loss and diarrhea, it is known locally as slim disease. It is strongly associated with HTLV-III infection (63 out of 71 patients) and affects females nearly as frequently as males. The clinical features are similar to those of enteropathic acquired immunodeficiency syndrome as seen in neighboring Zaire. However, the syndrome is rarely associated with Kaposi's sarcoma (KS), although KS is endemic in this area of Uganda. Slim disease occurs predominantly in the heterosexually promiscuous population. There is no clear evidence to implicate other possible means of transmission, such as by insect vectors or re-used injection needles. The site and timing of the first reported cases suggest that the disease arose in Tanzania.

Heterosexually Acquired HTLV-III/LAV Disease (AIDS-Related Complex and AIDS). Epidemiologic Evidence for Female-to-Male Transmission

R.R. Redfield, P.D. Markham, S.Z. Salahuddin, D.C. Wright, M.G. Sarngadharan and R.C. Gallo. JAMA 1985 Oct 18;254(15):2094-6.

Thirty-seven percent (15/41) of patients with human T-cell lymphotropic virus type III (HTLV-III) disease (acquired immunodeficiency syndrome (AIDS) or AIDS-related complex) sequentially evaluated at Walter Reed Army Medical Center, Washington, DC, acquired this infection from a partner(s) of the opposite sex. Demographic features of these 15 patients (ten males and five females) differed substantially from those for patients reported to the Centers for Disease Control. Heterosexual contact with partners who developed AIDS or who were at risk for AIDS was confirmed in six patients. The remaining nine patients had multiple (greater than 50) heterosexual partners and/or sexual contact with prostitutes. The method of sexual activity did not appear to be related to disease acquisition; however, this study clearly demonstrated that receptive anal intercourse was not a requirement. The observations reported herein provide further epidemiologic evidence to support the occurrence of bidirectional heterosexual transmission (both male-to-female and female-to-male) of HTLV-III infection and disease.

HTLV-III Infection among Health Care Workers. Association with Needle-Stick Injuries

S.H. Weiss, W.C. Saxinger, D. Rechtman, M.H. Grieco, J. Nadler, S. Holman, H.M. Ginzburg, J.E. Groopman, J.J. Goedert, P.D. Markham, et al. JAMA 1985 Oct 18;254(15):2089-93.

Health care workers are caring for an increasing number of persons infected with human T-cell lymphotropic virus type III (HTLV-III), the primary etiologic agent of the acquired immunodeficiency syndrome (AIDS). We studied 361 health care and clinical laboratory personnel from institutions in several metropolitan areas with both high and moderate levels of HTLV-III infection among high-risk group members to evaluate routes of exposure to and seropositivity for HTLV-III. Protection of the privacy of subjects and prospective determination of risk factors were integral components of the study design. Six (26%) of 23 health care workers with recognized risk factors for AIDS had HTLV-III antibodies. Thirty-nine (14%) of 278 workers at one institution, as well as a total of five workers from other institutions, reported possible percutaneous exposure to HTLV-III, usually injuries with needles that had been used on AIDS patients. There were three HTLV-III seropositive subjects who reported possible parenteral exposure to HTLV-III but no recognized AIDS risk factors. One was a symptomatic female, subject A, and her apparent sources of HTLV-III exposure were two puncture wounds, without injection of blood, made with needles used on AIDS patients. Human T-cell lymphotropic virus type III was cultured from her asymptomatic, seronegative long-term sexual partner, apparently representing female-to-male transmission. For the two other seropositive workers (subjects B and C) with nosocomial parenteral exposure, we could not rule out heterosexual transmission as a possible source of HTLV-III exposure. These latter two cases, as well as the identification of seropositive health care providers from known risk groups, point to the need for thorough case investigation to identify routes of exposure in health care workers. The risk of nosocomial HTLV-III transmission appears to be low and related to percutaneous exposure. Medical personnel should be trained systematically in the proper techniques and handling of instruments for phlebotomy and similar procedures to decrease occupational exposure to HTLV-III.

Seroepidemiology of Human T-Lymphotropic Virus Type III Among Homosexual Men with the Acquired Immunodeficiency Syndrome or Generalized Lymphadenopathy and Among Asymptomatic Controls in Boston

J.E. Groopman, K.H. Mayer, M.G. Sarngadharan, D. Ayotte, A.L. Devico, R. Finberg, A.H. Sliski, J.D. Allan and R.C. Gallo. Ann Intern Med 1985 Mar;102(3):334-7

We studied a cohort of 45 homosexual men with the acquired immunodeficiency syndrome, 78 with persistent unexplained generalized lymphadenopathy, and 160 asymptomatic homosexual controls for serologic evidence of infection with human T-lymphotropic virus type III (HTLV-III). Study participants were recruited from a community-based health center and a university hospital practice. Ninety-eight percent of men with the syndrome and greater than 90 percent of men with generalized lymphadenopathy had antibody to HTLV-III, while 21 percent of the controls were positive (p less than 0.001). Six patients with generalized lymphadenopathy developed the acquired immunodeficiency syndrome over 2 years; all were seropositive for HTLV-III. Thirty-six asymptomatic controls had had sexual contact with a man with the syndrome; receptive anal intercourse in this group was associated with seropositivity for HTLV-III. These data suggest that persistent generalized lymphadenopathy and the acquired immunodeficiency syndrome are part of a clinical spectrum of HTLV-III infection and that most high-risk homosexual men in some regions of the United States have not yet been infected with this virus.

HTLV-III Serology Distinguishes Atypical and Endemic Kaposi's Sarcoma in Africa

A.C. Bayley, R.G. Downing, R. Cheingsong-Popov, R.S. Tedder, A.G. Dalgleish and R.A. Weiss. Lancet 1985 Feb 16;1(8425):359-61

Serum samples from African patients with Kaposi's sarcoma and acquired immunodeficiency syndrome-related (AIDS-related) disorders and from normal subjects in Uganda and Zambia were tested for antibodies to the human T-lymphotropic retroviruses (HTLV) types I, II, and III. Nearly 90 percent of patients with AIDS-related disorders or with atypical, aggressive Kaposi's sarcoma were seropositive for HTLV-III in both countries, whereas only 17 percent of patients with classic endemic Kaposi's sarcoma were seropositive. Among the controls, 20 percent were seropositive for HTLV-III in Uganda but only 2 percent in Zambia. None of the subjects tested had antibodies to HTLV-I or HTLV-II. These results are further evidence of the emergence of a clinically atypical form of Kaposi's sarcoma in Africans, which resembles that seen in American patients with AIDS, and which is associated with HTLV-III infection. The low frequency of antibodies to HTLV-III in the normal Zambian population, together with the first appearance of HTLV-III-associated diseases during the past 2 years, suggests that this virus is new to Zambia, although it may have been present in Uganda for longer.

Relation of HTLV-III Seropositivity and Lymphadenopathy

E. Jeffries, W.J. Boyko, B. Willoughby, P.D. Constance, B. Wiggs, M. O'Shaughnessy and F.R. Sharp. Can Med Assoc J 1985 Jul 15;133(2):111-2.

Testing for antibody to human T-lymphotropic retrovirus (HTLV-III) was carried out in five groups of homosexual men: 250 without lymphadenopathy (control group), 37 with slight or nonpersistent lymph node enlargement (intermediate group), 141 with persistent generalized lymphadenopathy, 32 with persistent generalized lymphadenopathy who underwent biopsy, and 11 in whom acquired immune deficiency syndrome (AIDS) was diagnosed. The rates of HTLV-III seropositivity in the five groups were 18 percent, 32 percent, 61 percent, 94 percent and 91 percent, respectively.

Sexually Transmitted Diseases, T Cell Subsets, and Sexual Practices in Homosexual Men Attending an STD Clinic

R.D. Maw, J.H. Connolly, K. McFerran, J.N. McKirgan, T.A. McNeill, J.D. Merrett and J.D. Russell. Genitourin Med 1985 Jun;61(3):197-201.

Sixty-three homosexually active men and 42 heterosexual men answered questionnaires regarding aspects of their social life and sexual practices. Assessment of past sexually transmitted disease showed the homosexual group to have had a significantly greater incidence of syphilis, gonorrhea, perianal warts, and cytomegalovirus infections. T cell subset counts were carried out, and results for 60 of the homosexual men and 39 of the heterosexual men showed that the homosexuals had a significantly greater mean T cell suppressor cell count ($p = 0.0019$). The mean T helper cell count was not significantly different between the two groups, but it was significantly more ($p = 0.033$) in the more promiscuous homosexuals (who had more than 20 sexual partners a year) than in the heterosexuals. No relation was found between T cell subset counts and evidence of past cytomegalovirus infection. The practice of passive anal intercourse, oroanal sex, and swallowing semen during oral sex did not appear to influence T cell subset counts in the homosexuals.

Incidence of the Acquired Immunodeficiency Syndrome in San Francisco, 1980-1983

A.R. Moss, P. Bacchetti, D. Osmond, S. Dritz, D. Abrams, M. Conant, P. Volberding and J. Ziegler. J Infect Dis 1985 Jul;152(1):152-61.

Incidence data for the acquired immunodeficiency syndrome (AIDS) are presented on the basis of a surveillance file maintained by the San Francisco Bureau of Communicable Disease Control. The incidence of AIDS among residents of San Francisco rose steadily from the first case diagnosed in the last quarter of 1980 through the last quarter of 1983. New cases were diagnosed at a rate of 25 per month in the last quarter of 1983. Reported incidence declined in mid-1983, but the decline was probably a case-finding artifact. Smoothed incidence rates show a steady progressive rise, which is approximated equally well by quadratic or exponential curves. Among the patients diagnosed in San Francisco, 99 percent were homosexual or bisexual men. The cumulative incidence rate among homosexual or bisexual men was estimated to be 770 per 100,000 in the last quarter of 1983. The incidence rate of AIDS increased with age, and the increase was greater than that found with other sexually transmitted diseases. The difference in the age distributions between cases of AIDS and syphilis suggests either that susceptibility to AIDS increases with age or that the average latency associated with AIDS is longer than previously thought.

Acquired Immunodeficiency Syndrome (AIDS) in an Economically Disadvantaged Population

S. Maayan, G.P. Wormser, D. Hewlett, S.N. Miller, F.P. Duncanson, A. Rodriguez, E.N. Perla, B. Koppel and E.E. Rieber. Arch Intern Med 1985 Sep;145(9):1607-12.

Forty patients with acquired immunodeficiency syndrome (AIDS), 70 percent of whom were intravenous drug abusers (IVDAs), were seen over a 20-month period (July 1, 1981 through February 28, 1983). Most of the patients came from two inner-city sections of New York City and from nearby correctional facilities. Eighty-five percent of the patients were black or Hispanic; only 15 percent were white. Unique features of AIDS in this mostly heterosexual population were the high incidence of opportunistic infections (90% of the patients), the low incidence of Kaposi's sarcoma (10%), and the high mortality rate (34% died during initial hospitalization, 74% after one year of follow-up). Tuberculosis occurred in 10 percent of cases, preceding other opportunistic infections by four to 24 months. We found that AIDS was a common disease among inpatient IVDAs, and in one of the participating hospitals, its incidence was similar to that of infective endocarditis. Acquired immunodeficiency syndrome should be considered as the underlying illness in all IVDAs with oral thrush, shortness of breath, pneumonia, or extra-pulmonary tuberculosis.

Immediate Causes of Death in Acquired Immunodeficiency Syndrome

L. Moskowitz, G.T. Hensley, J.C. Chan and K. Adams. Arch Pathol Lab Med 1985 Aug;109(8):735-8.

We evaluated the immediate causes of death in 54 adults who underwent an autopsy and were diagnosed as having died of the acquired immunodeficiency syndrome between April 1980 and October 1983. The study group included 25 Haitians, 19 homosexual men, five intravenous drug abusers, two hemophiliacs (type A), and three with no known risk. Fourteen died of central nervous system diseases: 11 of *Toxoplasma encephalitis*, one of progressive multifocal leukoencephalopathy, one of viral encephalitis, and one of intracerebral hemorrhage. Thirty died of respiratory failure; 16 of *Pneumocystis carinii* pneumonia, ten of cytomegalovirus pneumonia, one of multiple infections, one of interstitial pneumonia, and two of bacterial pneumonia. Two died of overwhelming generalized infections: one of *Mycobacterium avium-intracellulare* and one of listeriosis. Six died of disseminated Kaposi's sarcoma, while the remaining two persons died of *Toxoplasma myocarditis* (one) and one of shock resulting from a percutaneous liver biopsy, respectively. There were differences in the immediate causes of death between Haitians and homosexuals as follows: 63 percent of homosexual men died of either *P. carinii* pneumonia or Kaposi's sarcoma vs. 20 percent of Haitians. In contrast, 72 percent of Haitians died of other opportunistic infections as compared with 21 percent of homosexuals. There has not been an increase in the proportion of cases diagnosed premortem since 1982 and overall, only 32 (58%) were diagnosed premortem; the rest were diagnosed only at autopsy. This study provided evidence that 42 percent died of currently untreatable diseases.

Acquired Immunodeficiency Syndrome. Clinicopathologic Study of 56 Autopsies

G.W. Niedt and R.A. Schinella. Arch Pathol Lab Med 1985 Aug;109(8):727-34.

We studied 56 patients with acquired immunodeficiency syndrome who underwent autopsy at the New York University Medical Center. We uncovered several entities that were not previously described or emphasized in prior series. These were as follows: (1) three cases of necrotizing arteritis with cytomegalovirus inclusions; (2) dissemination in 95 percent of cases of Kaposi's sarcoma; (3) unusual clinical and histologic presentations of Kaposi's sarcoma presenting diagnostic difficulties for both clinicians and pathologists; and (4) a very high incidence of serious nonmycobacterial infections. In addition, previous autopsy studies have disagreed over such matters as the incidence of disseminated candidiasis, hemophagocytosis, and severe adrenal necrosis in acquired immunodeficiency syndrome. All of these studies, except one, involved ten to 12 cases each. Our study of 56 cases helps to resolve these disagreements.

The Acquired Immunodeficiency Syndrome in a Cohort of Homosexual Men. A Six-Year Follow-Up Study

H.W. Jaffe, W.W. Darrow, D.F. Echenberg, P.M. O'Malley, J.P. Getchell, V.S. Kalyanaraman, R.H. Byers, D.P. Drennan, E.H. Braff, J.W. Curran, et al. Ann Intern Med 1985 Aug;103(2):210-4.

A cohort of 6,875 homosexual men, initially seen at the San Francisco City Clinic between 1978 and 1980, were studied to determine the incidence and prevalence of the acquired immunodeficiency syndrome, related conditions, and infection with the human T-lymphotropic virus, type III/lymphadenopathy-associated virus (HTLV-III/LAV). By December 1984, 2.4 percent of the men had the syndrome; mortality attributable to the syndrome in 1984 was 600/100 000. For each man with the syndrome in a representative sample of 474 cohort members seen in 1984, 7.5 men had generalized lymphadenopathy, 1.1 had other prodromal findings, and 0.8 had hematologic abnormalities. Prevalence of serum antibodies to HTLV-III/LAV, measured by an enzyme-linked immunosorbent assay, increased from 4.5 percent in 1978 to 67.4 percent in 1984. Of 31 persons who were seropositive and without the syndrome between 1978 and 1980, two developed the syndrome and eight developed related conditions during a median follow-up of 61 months. Over a 6-year period, two-thirds of cohort members were infected with HTLV-III/LAV and almost one-third developed related conditions.

Unexplained Persistent Lymphadenopathy in Homosexual Men and the Acquired Immune Deficiency Syndrome

J.W. Gold, C.S. Weikel, J. Godbold, C. Garcia, C. Urmacher, S. Cunningham-Rundles, B. Koziner, M. Pollack, R.C. Gallo, M.G. Sarngadharan, et al. Medicine (Baltimore) 1985 May;64(3):203-13.

Ninety-three homosexual men with persistent lymphadenopathy were followed at the Memorial Sloan-Kettering Cancer Center for a mean period of 20.8 months. Histories and serologic evidence of a number of previous infections were common, but the lymphadenopathy was not due to recognizable infections or neoplastic disease. Leukopenia, lymphopenia, granulocytopenia, monocytopenia, decreased ratios of T-helper to T-suppressor cells, decreased natural killer cell activity, and increased serum immunoglobulin concentrations were common. Lymph node biopsies showed reactive hyperplasia without any unique histopathologic features. Antibody to the human T-lymphotropic virus-III (HTLV-III or LAV), a newly described retrovirus believed to be the etiologic agent of the acquired immune deficiency syndrome (AIDS), was detected in 91.4 percent. Over a 3-year period, 11 cases of AIDS were recognized in these patients: Kaposi's sarcoma developed in seven and opportunistic infections in four. The lymphadenopathy resolved in six patients and the others remained unchanged. Although most of these patients are asymptomatic and remain well, the risk of AIDS in this group of men was higher than in other groups of homosexual men in New York.

Evidence for Exposure to HTLV-III in Uganda Before 1973

W.C. Saxinger, P.H. Levine, A.G. Dean, G. de The, G. Lange-Wantzin, J. Moghissi, F. Laurent, M. Hoh, M.G. Sarngadharan and R.C. Gallo. Science 1985 Mar 1;227(4690):1036-8.

Fifty of 75 serum samples collected in the West Nile district of Uganda between August 1972 and July 1973 contained antibodies reactive with human T-cell leukemia (lymphotropic) virus type 3 (HTLV-III; mean titer, 601), while 12 of 75 samples were positive in a similar test for HTLV type 1 (HTLV-1) antibodies (mean titer, 236). The samples were screened by enzyme-linked immunosorbent assay and positive results were confirmed by a newly developed unlabeled antibody-peroxidase procedure with enhanced sensitivity for detection of antibody binding to immunoblots of HTLV-III antigen, demonstrating antibodies to proteins with molecular weights of 24,000, 41,000, and 76,000 in nearly all positive samples. Analysis of titration data indicated enhanced titers of antibody against HTLV-III and HTLV-I when coinfection occurred. The high prevalence and relatively low titers (compared to serum from patients with acquired immune deficiency syndrome (AIDS)) of antibodies recognizing HTLV-III proteins in sera from this population at a time that may predate or coincide with the appearance or spread of the AIDS agent (HTLV-III) suggest that the virus detected may have been a predecessor of HTLV-III or is HTLV-III itself but existing in a population acclimated to its presence. It further suggests an African origin of HTLV-III.

Spectrum of Pulmonary Diseases Associated with the Acquired Immune Deficiency Syndrome

D.E. Stover, D.A. White, P.A. Romano, R.A. Gellene and W.A. Robeson. Am J Med 1985 Mar;78(3):429-37.

Over a four-year period, 130 patients with the acquired immune deficiency syndrome were studied to assess the incidence and spectrum of pulmonary disease associated with this illness. In 61 patients (47%), respiratory abnormalities were either present on admission or later developed. Multiple pathologic processes were present simultaneously in 24 patients and serial pulmonary problems developed in seven patients. Infection was the most common cause of pulmonary parenchymal disease and was due to *Pneumocystis carinii* (35 patients), cytomegalovirus (21 patients), *Mycobacterium avium*-intracellulare (13 patients), and bacteria (4 patients). Noninfectious causes of parenchymal lung diseases were also frequently seen and included Kaposi's sarcoma (eight patients), nonspecific pneumonitis (seven patients), and adult respiratory distress syndrome (four patients). Significant pleural disease was present in six cases and was usually related to Kaposi's sarcoma. A bronchospastic disorder developed in four patients. Pulmonary function tests, in particular the diffusing capacity and the difference between rest and exercise alveolar-arterial oxygen tension, were helpful in screening for pulmonary diseases. Patterns of clinical features and radiographic abnormalities were recognized and suggested specific diagnoses. Overall mortality from respiratory causes identified during the study was 41 percent, but varied markedly with the etiologic agent. Respiratory failure, however, carried a 100 percent mortality despite the underlying cause.

The Radiographic Appearance of Tuberculosis in Patients with the Acquired Immune Deficiency Syndrome (AIDS) and Pre-AIDS

A.E. Pitchenik and H.A. Rubinson. Am Rev Respir Dis 1985 Mar;131(3):393-6.

We reviewed the medical records and chest radiographs of 23 adult patients with culture-proved tuberculosis and verified acquired immune deficiency syndrome. Seventeen patients, including 8 with disseminated tuberculosis, had positive sputum or bronchial washing cultures for *Mycobacterium tuberculosis*. Their initial pretreatment radiographs revealed hilar and/or mediastinal adenopathy in 10 patients (59%), localized pulmonary infiltrates limited to the middle or lower lung fields in 5 patients (29%), localized pulmonary infiltrates involving an upper lobe in 3 patients (18%), diffuse miliary or interstitial infiltrates in 3 patients (18%), no pulmonary infiltrates in 6 patients (35%), and no abnormalities in 2 patients (12%). Pulmonary cavitation was not seen. Only 1 patient (6%) had a chest radiograph typical of adult onset reactivation tuberculosis (i.e., localized pulmonary infiltrate involving the upper lung fields without hilar or mediastinal adenopathy). Six patients (35%) had pulmonary infiltrates that may have been caused by concomitant nontuberculous infection. Six patients had positive cultures for *M. tuberculosis* from extrapulmonary sites only. Three (50%) of these patients had hilar and/or mediastinal adenopathy. None of them had pulmonary infiltrates on their initial chest radiograph.

Frequent Transmission of HTLV-III among Spouses of Patients with AIDS-Related Complex and AIDS

R.R. Redfield, P.D. Markham, S.Z. Salahuddin, M.G. Sarngadharan, A.J. Bodner, T.M. Folks, W.R. Ballou, D.C. Wright and R.C. Gallo. JAMA 1985 Mar 15;253(11):1571-3.

Seven cases of acquired immunodeficiency syndrome (AIDS) and AIDS-related complex (ARC) associated with human T-cell leukemia (lymphotropic) virus (HTLV)-III infection were documented in married males whose family members consented to medical evaluation. Five spouses also had evidence of HTLV-III infection documented by isolation of virus and by detection of serum antibody directed against viral structural proteins. Three of the five HTLV-positive spouses also had clinical evidence of ARC. The remaining four spouses were clinically healthy. Eleven children (between 14 months and 13 years of age) were also evaluated for evidence of disease and exposure to HTLV-III. Only one 14-month-old child was seropositive for antibody to HTLV-III. These data support the opinion that close household contact to patients with ARC or AIDS is not an efficient mechanism for virus transmission, while demonstrating that HTLV-III can be transmitted by repeated heterosexual contact.

Acute AIDS Retrovirus Infection. Definition of a Clinical Illness Associated with Seroconversion

D.A. Cooper, J. Gold, P. Maclean, B. Donovan, R. Finlayson, T.G. Barnes, H.M. Michelmore, P. Brooke and R. Penny. Lancet 1985 Mar 9;1(8428):537-40.

In the course of a prospective immunoepidemiological study of homosexual men in Sydney, seroconversion to the AIDS-associated retrovirus (ARV) was observed in 12 subjects. Review of the clinical files defined an acute infectious-mononucleosis-like illness in 11 subjects. The illness was of sudden onset, lasted from 3 to 14 days, and was associated with fevers, sweats, malaise, lethargy, anorexia, nausea, myalgia, arthralgia, headaches, sore throat, diarrhea, generalized lymphadenopathy, a macular erythematous truncal eruption, and thrombocytopenia. In 1 subject, an incubation period of 6 days after presumed exposure to ARV was determined and in 3 subjects seroconversion took place 19, 32, and 56 days after onset. Comparison of T-cell subsets before and after the acute illness showed inversion of T4:T8 ratio in 8 subjects, due to increased numbers of circulating T8+ cells. These findings support the notion of an acute clinical, immunological, and serological response to infection with ARV which should be considered in the differential diagnosis of mononucleosis-like syndromes in groups at high risk for the development of AIDS.

Antibody to Human T-Lymphotropic Virus Type III in Wives of Hemophiliacs. Evidence for Heterosexual Transmission

J.K. Kreiss, L.W. Kitchen, H.E. Prince, C.K. Kasper and M. Essex. Ann Intern Med 1985 May;102(5):623-6.

To evaluate the risk of heterosexual transmission of the acquired immunodeficiency syndrome, lymphadenopathy, and infection with human T-lymphotropic virus type III (HTLV-III), we studied 42 hemophiliacs and their wives. By early 1984, 9 of the hemophiliacs had asymptomatic lymphadenopathy and 1 had the acquired immunodeficiency syndrome. Twenty-one hemophiliacs, including all 10 with clinically overt disease, had antibody to HTLV-III. None of the 42 wives had lymphadenopathy or the acquired immunodeficiency syndrome but 2 had HTLV-III antibody. One of these women had evidence of immunologic dysfunction with a markedly reduced T-helper/suppressor cell ratio. The husbands of these 2 women both had HTLV-III antibody, but neither had overt acquired immunodeficiency syndrome-related disease. Thus, as of early 1984, the prevalence of HTLV-III antibody in wives of hemophiliacs seropositive for HTLV-III was 9.5 percent (2 of 21). We conclude that transmission of HTLV-III occurs between hemophiliacs and their heterosexual partners.

AIDS and Sexual Behavior Reported by Gay Men in San Francisco

L. McKusick, W. Horstman and T.J. Coates. Am J Public Health 1985 May;75(5):493-6.

In November 1983, we surveyed 655 gay men in San Francisco regarding their sexual practices during the previous month and the same month one year ago. The sample was selected to include men in situations that would lead to high risk of sexual activities related to AIDS (acquired immune deficiency syndrome) transmission (i.e., men frequenting bathhouses and gay bars), as well as men in low-risk situations (those going to neither place and men in primary relationships). The Bath group showed little change in frequency of bathhouse use and in number of sexual partners from that location. The other groups showed substantial reductions in frequency of sexual contacts from bars, baths, T-rooms, or parks. Men in monogamous relationships showed little change in sexual behavior within their relationship. Men in non-monogamous relationships and men not in relationships reported substantial reductions in high-risk sexual activity, but not a corresponding increase in low-risk sexual behavior. Knowledge of health guidelines was quite high, but this knowledge had no relation to sexual behavior. Using sex to release tension, use of sex to express gay identity, and knowledge of persons with AIDS in the advanced stages of disease were related to frequency and type of sexual behavior.

Retrovirus-Like Particles in Salivary Glands, Prostate and Testes of AIDS Patients

G. Lecatsas, S. Houff, A. Macher, E. Gelman, R. Steis, C. Reichert, H. Masur and J.L. Sever. Proc Soc Exp Biol Med 1985 Apr;178(4):653-5.

AIDS associated retrovirus-like particles were identified in the salivary gland, prostate and/or testicle of two AIDS patients. These findings further suggest that saliva and semen may transmit the infection to susceptible individuals.

Safety of Human Blood Products: Inactivation of Retroviruses by Heat Treatment at 60 Degrees C

J. Hilfenhaus, R. Mauler, R. Friis and H. Bauer. Proc Soc Exp Biol Med 1985 Apr;178(4):580-4.

Acquired immune deficiency syndrome (AIDS) can be transferred to patients by blood transfusions or human blood preparations, such as cryoprecipitates or factor VIII concentrates. Retroviruses have been discussed as infectious AIDS agents and more recently human T-lymphotropic retroviruses designated as HTLV type III and LAV (lymphadenopathy-associated virus) have been isolated from AIDS patients. Whether heat treatment at 60 degrees C (pasteurization) of liquid human plasma protein preparations inactivates retroviruses was, therefore, investigated. Pasteurization had already been included in the routine manufacturing process of human plasma protein preparations in order to guarantee safety with regard to hepatitis B. Since high titer preparations of human retroviruses were not available, heat inactivation was studied using Rous sarcoma virus added to the various plasma protein preparations tested. This retrovirus which was obtained in preparations of 6.0 log10 FFU/ml was shown to be at least as heat stable as two mammalian retroviruses studied, i.e., feline and simian sarcoma virus. In all of eight different plasma protein preparations tested, Rous sarcoma virus was completely inactivated after a heat treatment lasting no longer than 4 hours. It is thus concluded that pasteurization of liquid plasma protein preparations at 60 degrees C over a period of 10 hours must confer safety to these products with respect to AIDS, provided that the AIDS agents are retroviruses of comparable heat stability as Rous sarcoma virus and the mammalian retroviruses tested.

Postnatal Transmission of AIDS-Associated Retrovirus from Mother to Infant

J.B. Ziegler, D.A. Cooper, R.O. Johnson and J. Gold. Lancet 1985 Apr 20;1(8434):896-8.

The third child of a previously healthy woman was delivered by caesarean section. Because of intraoperative blood loss, a blood transfusion was given after the delivery. The baby was breast-fed for 6 weeks. One unit of blood came from a male in whom the acquired immunodeficiency syndrome (AIDS) developed 13 months later. On recall, the mother proved to have lymphadenopathy, serum antibody to the AIDS virus, and a reduced T4/T8 ratio. The infant, who failed two thrive and had atopic eczema from 3 months, has likewise proved to have antibody to the AIDS virus. Since his mother was transfused after his birth, he is presumed to have been infected via breast milk or by way of some other form of close contact with his mother.

Increase in High-Grade Lymphomas in Young Men

C.C. Boring, R.K. Brynes, W.C. Chan, N. Causey, H.R. Gregory, M.R. Nadel and R.S. Greenberg. Lancet 1985 Apr 13;1(8433):857-9.

The relative frequencies of non-Hodgkin's lymphoma (NHL) subtypes and primary sites of presentation in young men before and during the acquired immunodeficiency syndrome epidemic were studied. Diagnostic pathological specimens were reviewed and classified according to the Working Formulation grades for cases of NHL in men aged 20-49 years identified through a population-based cancer registry. Seventy-six percent of the lymphomas diagnosed in 1981-82 were intermediate or high grade, compared with 29 percent of those diagnosed in 1976-77. This increase was still significant when men aged 20-39 years and 40-49 years were grouped separately, and for married men. The proportion of extranodal lymphomas diagnosed in men aged 20-39 years also rose significantly from the early to the later period.

Seroepidemiology of HTLV-III Antibodies in a Remote Population of Eastern Zaire

R.J. Biggar, M. Melbye, L. Kestens, M. de Feyter, C. Saxinger, A.J. Bodner, L. Paluko, W.A. Blattner and P.L. Gigase. Br Med J (Clin Res) 1985 Mar 16;290(6471):808-10.

A human retrovirus—human T cell lymphotropic virus-III (HTLV-III)—has recently emerged as the probable cause of acquired immunodeficiency syndrome (AIDS). In May 1984, 250 outpatients at a hospital in a remote area of eastern Zaire were surveyed for AIDS type illnesses and the prevalence of antibodies against HTLV-III determined by an enzyme linked immunosorbent assay using disrupted whole HTLV-III virus as the antigen. No clinical cases of AIDS were diagnosed among these patients. Overall, 31 (12.4%) had clearly positive ratios (greater than or equal to 5.0) and a further 30 (12.0%) had borderline ratios (3.0- less than 5.0). Western blots of serum samples from subjects with antibodies yielded bands consistent with HTLV-III as found in American patients with AIDS and members of groups at risk of AIDS. The prevalence of antibody was highest in childhood ($p = 0.02$); among adults prevalence rose slightly with age. HTLV-III antibodies were more common among the uneducated ($p = 0.006$), agricultural workers ($p = 0.03$), and rural residents ($p = 0.006$), but the Western blot bands were generally weak in this group. By contrast, one urban resident had strong bands. The relatively high prevalence of antibodies among the rural poor in this area of Zaire suggests that HTLV-III or a closely related, cross reactive virus may be endemic in the region. A different natural history of infection, perhaps in childhood, may also explain the findings.

Acquired Immunodeficiency Syndrome in the Child of a Hemophiliac

M.V. Ragni, A.H. Urbach, S. Kiernan, J. Stambouli, B. Cohen, B.S. Rabin, A. Winkelstein, J.C. Gartner, B.Z. Zitelli, J.J. Malatack, et al. Lancet 1985 Jan 19;1(8421):133-5

Oral thrush developed during the second month of life in the 5-month-old son of a patient with hemophilia A. He did not feed well, and interstitial pneumonitis, lymphadenopathy, hepatosplenomegaly, and a cellular immune defect consistent with the acquired immunodeficiency syndrome (AIDS) followed. Both parents had signs of pre-AIDS during the year before their son's illness. Transmission presumably occurred in three steps: parenterally, via factor VIII concentrate in the hemophiliac; heterosexually, from the hemophiliac to his wife; and vertically, from mother to infant, or via close paternal-infant or maternal-infant contact. This first report of AIDS in the child of a hemophiliac supports the theory that AIDS is caused by an infectious agent. Concentrate-treated hemophiliacs may transmit this agent to their spouses or children, resulting in pre-AIDS or AIDS.

Acquired Immune Deficiency Syndrome in Childhood

K.M. Shannon and A.J. Ammann. J Pediatr 1985 Feb;106(2):332-42

The acquired immunodeficiency syndrome has been observed with increasing frequency in children with associated hemophilia, high-risk environmental backgrounds, and blood transfusions. AIDS should be considered in the differential diagnosis of childhood immunodeficiency, and it must be distinguished from congenital disorders. We emphasize the importance of epidemiologic, clinical, and laboratory data in diagnosis and aggressive management of infectious complications. The relationship between human retrovirus infection and AIDS remains to be precisely defined, especially with regard to cofactors that may play a role in the development of severe immunodeficiency following exposure to the agent.

Laboratory Diagnosis

Importance of Western Blot Analysis in Predicting Infectivity of Anti-HTLV-III/LAV Positive Blood

J.I. Esteban, J.W. Shih, C.C. Tai, A.J. Bodner, J.W. Kay and H.J. Alter. Lancet 1985 Nov 16;2(8464):1083-6.

Stored donor and recipient sera from prospective studies of post-transfusion hepatitis were analyzed for the presence of human T-cell lymphotropic virus type-III/lymphadenopathy associated virus (HTLV-III/LAV) antibodies as determined by enzyme-linked immunosorbent assays (ELISA). Of 3,961 donor samples given to 461 patients, only 2 (0.05%) contained specific HTLV-III/LAV antibodies as determined by an avidin-biotin-enhanced western blot technique. Anti-HTLV-III/LAV was measured before and 3 and 6 months after transfusion in 295 recipients of anti-HTLV-III-negative blood, seven recipients of ELISA-positive blood which was western blot negative, and two recipients of ELISA-positive blood confirmed as specific by western blot. Only the last two recipients became infected with HTLV-III/LAV, as assessed by antibody seroconversion (p less than 0.0001). Seroconversion occurred early (6 and 8 weeks after transfusion) and was characterized first by antibody to p24 and later by antibody to p41.

AIDS has not developed in either patient, but one has a T4/T8 ratio of 0.4 and impaired mitogen responses; the second patient has no evidence of immune dysfunction 4 years after exposure. This study confirms that HTLV-III/LAV infection can be transmitted by blood transfusion and supports the advisability of anti-HTLV-III/LAV testing of all blood donors. It also confirms the validity of western blot testing for HTLV-III/LAV specificity and suggests that ELISA-positive, western-blot-negative blood may not be infectious.

AIDS and Hemophilia: Morbidity and Morality in a Well Defined Population

P. Jones, P.J. Hamilton, G. Bird, M. Fearns, A. Oxley, R. Tedder, R. Cheingsong-Popov and A. Codd. Br Med J (Clin Res) 1985 Sep 14;291(6497):695-9.

One hundred and forty-three multitransfused patients with hereditary hemostatic disorders were examined for evidence of disease related to the acquired immune deficiency syndrome (AIDS). Ninety-nine patients with severe hemophilia A were tested for anti-HTLV-III and 76 were found to be positive. All except one of these seropositive patients had received commercial factor VIII concentrates at some time. Eighteen patients with hemophilia B were tested and all were anti-HTLV-III negative. Three out of 36 sexual partners of patients with hemophilia A positive for anti-HTLV-III were also seropositive. One, who had recently received blood transfusions, had AIDS with *Pneumocystis carinii* pneumonia. Three patients with severe hemophilia A died from AIDS. A further 30 hemophiliacs had AIDS related complex or lymphadenopathy that could be related to HTLV-III infection. There was a significant correlation between lymphadenopathy and anti-HTLV-III seropositivity. No evidence of casual spread of AIDS was found since all 68 health care staff tested were anti-HTLV-III negative, including three surgeons who regularly worked with patients positive for anti-HTLV-III. The resources devoted to counselling and laboratory support in centers treating people at risk and their families need to be urgently reassessed.

Screening Tests for Blood Donors Presumed to have Transmitted the Acquired Immunodeficiency Syndrome

J.S. McDougal, H.W. Jaffe, C.D. Cabridilla, M.G. Sarngadharan, J.K. Nicholson, V.S. Kalyanaraman, C.A. Schable, B. Kilbourne, B.L. Evatt, R.C. Gallo, et al. Blood 1985 Mar;65(3):772-5.

We investigated 18 sets of blood donors from 12 to 50 months after they donated blood to recipients who subsequently developed the acquired immunodeficiency syndrome (AIDS). Within each donor set, only one donor was suspected of having transmitted the disease (ie, member of an AIDS risk group). The other donors (n = 189) were not risk group members and served as controls. A number of laboratory tests distinguished suspected from nonsuspected donors, including determination of T helper/T suppressor cell ratio, antibody to hepatitis B core antigen, and immune complexes, but none of these was as sensitive and specific as tests for antibody to the human retrovirus, HTLV-III/LAV.

Therapy

The AIDS Epidemic: A Model for Developing Intervention Strategies for Reducing High-Risk Behavior in Gay Men

L. McKusick, M. Conant and T.J. Coates. Sex Transm Dis 1985 Oct-Dec;12(4):229-34.

The authors convened a conference at the University of California, San Francisco, to provide a framework for developing health education programs to reduce high-risk sexual activity associated with the acquired immunodeficiency syndrome (AIDS). Operating on a consensus model, four groups of experts defined the sexual behaviors that place an individual at high risk for AIDS, the principles of health psychology that can be applied to health education programs for reducing high-risk sexual activity among gay men, the health education and media strategies that might be used, and the factors unique to gay men that need to be considered. We hope that these reports will not only provide a foundation for the discussion of health education strategies for reducing the risk of AIDS, but will also prove useful to local, regional, and national organizations in developing such programs.

Effect of 9-(1,3-Dihydroxy-2-Propoxymethyl) Guanine on Serious Cytomegalovirus Disease in Eight Immunosuppressed Homosexual Men

H. Masur, H.C. Lane, A. Palestine, P.D. Smith, J. Manischewitz, G. Stevens, L. Fujikawa, A.M. Macher, R. Nussenblatt, B. Baird, et al. Ann Intern Med 1986 Jan;104(1):41-4.

Eight immunosuppressed homosexual men with cytomegalovirus viremia—seven with serious bilateral retinitis, one with colitis in addition to retinitis, and one with pneumonitis only—were treated with a new acyclovir derivative, 9-(1,3-dihydroxy-2-propoxymethyl) guanine, which has excellent in vitro activity against cytomegalovirus. All patients had virologic and clinical improvement, but substantial leukopenia developed in three patients. Both clinical relapses and viral relapses occurred frequently, usually within 30 days after cessation of treatment. 9-(1,3-Dihydroxy-2-propoxymethyl) guanine represents the first clinically and virologically effective agent for the treatment of cytomegalovirus disease, but more effective and less toxic therapeutic regimens for both acute and chronic use must be developed.

Prospects of Therapy for Infections with Human T-Lymphotropic Virus Type III

M.S. Hirsch and J.C. Kaplan. Ann Intern Med 1985 Nov;103(5):750-5.

Human T-lymphotropic virus type III is susceptible to attack at various sites during its replicative cycle. Inhibitors of reverse transcriptase activity, including suramin, antimoniotungstate (HPA-23), and trisodium phosphonoformate, have shown in vitro activity against the virus in early clinical trials. Other significant antiviral agents are recombinant interferon alpha-A, ribavirin, and ansamycin. Double-blind, placebo-controlled clinical trials of interferon alpha, which inhibits viral replication at easily achievable serum levels, are underway. The development of optimal therapeutic regimens will require carefully controlled, multicenter collaborative trials with standardized criteria for evaluating responses. Prolonged treatment with combinations of antiviral and immunomodulating agents may be necessary for control of HTLV-III replication and for effective treatment of the acquired immunodeficiency syndrome.

Preliminary Clinical Observations with Recombinant Interleukin-2 in Patients with AIDS or LAS

P. Kern, J. Toy and M. Dietrich. Blut 1985 Jan;50(1):1-6.

The toxicity of recombinant Interleukin-2 (IL-2) was studied in patients with acquired immunodeficiency syndrome (AIDS) or persistent lymphadenopathy syndrome (LAS). Increasing doses of the drug from 10(3) Units/m2 to 10(6) U/m2 were given as an intravenous bolus injection. At the high-dose levels some minor effects, such as fever up to 39.5 degrees C, chills, malaise or vomiting, were observed. The administration of 10(6) U/m2 as a 4-hour infusion showed identical results. No particular alterations of laboratory parameters were found. At the high-dose level the serum concentration of neopterin, which is released from macrophages after interferon gamma stimulation, was significantly (p less than 0.001) elevated above pretreatment levels. The clinical observation of daily infusions of 10(6)/m2 for 14 days revealed the same side effects. All patients developed lymphocytosis and eosinophilia. Two patients had suffered from severe diarrhea for several weeks presumably due to cryptosporidiosis. In both cases, diarrhea ceased under the treatment with IL-2 and did not occur in the following two months.

Research and Evaluation

Serological Evidence for Virus Related to Simian T-Lymphotropic Retrovirus III in Residents of West Africa

F. Barin, S. M'Boup, F. Denis, P. Kanki, J.S. Allan, T.H. Lee and M. Essex. Lancet 1985 Dec 21-28;2(8469-70):1387-9.

Serological evidence is presented here suggesting that a virus closely related to simian T-lymphotropic virus type III (STLV-III) infects man in Senegal, West Africa, a region where AIDS or AIDS-related diseases have not yet been observed. Twenty-five sera from Senegalese individuals that were positive for antibodies to HTLV-III by enzyme-linked immunosorbent assay were examined for antibodies to HTLV-III and STLV-III by western blotting. Sera from individuals originating from regions where AIDS has been reported, such as the United States and Burundi (central Africa), reacted best with antigens of HTLV-III, although antibodies that cross-reacted with STLV-III p24 were also detected. Conversely, sera originating from Senegalese people reacted better with STLV-III than with HTLV-III. This was exemplified by the absence of reactivity in sera from both monkeys and Senegalese people to p41, an antigen regularly detected by sera from antibody positive individuals originating from central Africa or from the United States. In contrast, sera from central Africa or the United States did not react with p32, the putative envelope transmembrane protein of STLV-III that is regularly detected by sera from both monkeys and antibody-positive Senegalese people. These results suggest that certain healthy Senegalese people have been exposed to a virus that is more closely related to STLV-III than to HTLV-III. The existence and study of such virus variants potentially with differential pathogenicity may provide important information for the development of an AIDS virus vaccine.

HTLV-III/LAV Antibody and Immune Status of Household Contacts and Sexual Partners of Persons with Hemophilia

J.M. Jason, J.S. McDougal, G. Dixon, D.N. Lawrence, M.S. Kennedy, M. Hilgartner, L. Aledort and B.L. Evatt. JAMA 1986 Jan 10;255(2):212-5.

We evaluated the human T-cell lymphotropic virus type III/lymphadenopathy-associated virus (HTLV-III/LAV) antibody and immune status of 88 persons living with and/or sexual partners of 43 hemophiliacs, 12 of whom had AIDS, five of whom had AIDS-related complex (ARC), 17 of whom were clinically well but HTLV-III/LAV antibody positive, and nine of whom were well and HTLV-III/LAV antibody negative. No nonhemophilic household contacts (0/50) of healthy hemophiliacs were HTLV-III/LAV antibody positive; two of 33 nonhemophilic AIDS/ARC contacts were positive. One was a spouse and one a sexual partner of a hemophiliac. One of these antibody-positive contacts herself had AIDS, and one had ARC. Antibody-negative, nonhemophilic contacts of AIDS/ARC and of antibody-positive hemophiliacs had significantly lower numbers of lymphocytes, T helper lymphocytes, and T suppressor lymphocytes than did contacts of antibody-negative hemophiliacs. We conclude that risk of HTLV-III/LAV transmission may exist for spouses and/or sexual contacts of hemophiliacs with AIDS/ARC, but we cannot now determine the risk for contacts of asymptomatic hemophiliacs.

The Economic Impact of the First 10,000 Cases of Acquired Immunodeficiency Syndrome in the United States

A.M. Hardy, K. Rauch, D. Echenberg, W.M. Morgan and J.W. Curran. JAMA 1986 Jan 10;255(2):209-11.

Acquired immunodeficiency syndrome (AIDS) is a serious, fatal disease affecting a relatively young population and has a great economic impact. Expenditures for hospitalization and economic losses from disability and premature death were estimated for the first 10,000 patients with AIDS reported in the United States. Extrapolation of data from surveys done in New York City, Philadelphia, and San Francisco suggests that these 10,000 patients with AIDS will require an estimated 1.6 million days in the hospital, resulting in over $1.4 billion in expenditures. Losses incurred for the 8,387 years of work that will be lost from disability and from the premature death of the 10,000 patients will be over $4.8 billion. The total economic burden of the AIDS epidemic will continue to rise as the number of diagnosed cases increases. These estimates reinforce the need for effective disease prevention strategies to reduce the number of cases.

Lymphadenopathy-Associated Virus: From Molecular Biology to Pathogenicity

L. Montagnier. Ann Intern Med 1985 Nov;103(5):689-93.

Recent data indicate that the lymphadenopathy-associated virus (LAV) is morphologically similar to animal lentiviruses, such as equine infectious anemia and visna viruses. This finding, together with the cross-reactivity of the core proteins of LAV with those of the equine infectious anemia virus and a similarity in genome structure and biological properties, allows LAV to be placed in the retroviral subfamily of Lentivirinae. Molecular data indicate a high degree of genetic variation of the virus, especially in the envelope gene, which have important implications for the origin of the virus (the T4 lymphotropism may be a recently acquired property) and for future immunization. Another problem is the role of viral infection in the induction of irreversible immunodeficiency. This syndrome occurs in a minority of infected persons, who generally have in common a past of antigenic stimulation and of immune depression before LAV infection.

Infection with HTLV-III/LAV and Transfusion-Associated Acquired Immunodeficiency Syndrome. Serologic Evidence of an Association

H.W. Jaffe, M.G. Sarngadharan, A.L. DeVico, L. Bruch, J.P. Getchell, V.S. Kalyanaraman, H.W. Haverkos, R.L. Stoneburner, R.C. Gallo and J.W. Curran. JAMA 1985 Aug 9;254(6):770-3.

We studied patients with transfusion-associated acquired immunodeficiency syndrome (AIDS) and their blood donors for serologic evidence of infection with human T-cell lymphotropic virus type III/lymphadenopathy-associated virus with two enzyme-linked immunosorbent assays and a Western blot assay. All 19 patients with AIDS were seropositive by at least one test. In all 28 donor sets containing "high-risk" donors, at least one donor was seropositive by one or more tests. Of 255 donors not considered high risk, two (0.8%) were seropositive by all three tests. When 30 seropositive high-risk donors were evaluated a median of 29 months after donation, four (13%) had developed AIDS and eight (27%) had lymphadenopathy. Our findings support the hypothesis that human T-cell lymphotropic virus type III/lymphadenopathy-associated virus causes AIDS and indicate that seropositive high-risk donors may be at relatively high risk for developing AIDS or related conditions themselves.

Acquired Immunodeficiency Syndrome in New York City. Evaluation of an Active Surveillance System

M.E. Chamberland, J.R. Allen, J.M. Monroe, N. Garcia, C. Morgan, R. Reiss, H. Stephens, J. Walker and S.M. Friedman. JAMA 1985 Jul 19;254(3):383-7.

In January 1983, the New York City Department of Health initiated an active surveillance program for acquired immunodeficiency syndrome (AIDS) in 19 hospitals and a modified-active surveillance program in the remaining 69 hospitals. We reviewed hospital laboratory and autopsy records in 12 active surveillance hospitals and three modified-active surveillance hospitals six months later. Patients who had opportunistic diseases characteristic of AIDS diagnosed in 1982 (before active surveillance) and 1983 (after implementation of active surveillance) were matched against health department AIDS surveillance reports. For the 16 months we evaluated, 96 percent of patients identified with AIDS in the 12 active surveillance hospitals and 100 percent of those in the three modified-active surveillance hospitals had been reported to the health department. The delay between diagnosing a case and reporting it to the health department significantly decreased between 1981 and the first six months of 1983 in all hospitals. The proportion of cases reported within one month of diagnosis increased from 45 percent to 69 percent during this period. We conclude that the current surveillance program for AIDS in New York City is effective and that case reporting is sufficiently complete for accurate analysis of disease trends.

Unexplained Lymphadenopathy in Homosexual Men. A Longitudinal Study

D.B. Fishbein, J.E. Kaplan, T.J. Spira, B. Miller, L.B. Schonberger, P.F. Pinsky, J.P. Getchell, V.S. Kalyanaraman and J.S. Braude. JAMA 1985 Aug 16;254(7):930-5.

In January 1982, the Centers for Disease Control began a prospective study of unexplained generalized lymphadenopathy syndrome in 78 homosexual or bisexual men. As of August 1, 1984, the median durations of lymphadenopathy and enrollment were 29.5 months and 20 months, respectively. Antibodies to human T-cell lymphotropic virus type III/lymphadenopathy-associated virus were present in 75 (96%) of the study patients. Five (6%) of the patients were diagnosed as having the acquired immunodeficiency syndrome five to 25 months after the onset of lymphadenopathy. At the time of their initial visit, these five patients had lower T-helper cell counts, hematocrits, lymphocyte counts, and pokeweed mitogen stimulation ratios and were more likely to report severe symptoms than patients who did not develop the acquired immunodeficiency syndrome. During 318 follow-up visits, except for the development of the acquired immunodeficiency syndrome in five patients, there has been little change in the initial laboratory and clinical measures of this cohort. Within the follow-up period of this study, the features of lymphadenopathy syndrome have been unremitting for the majority of patients.

Decreased Helper T Lymphocytes in Homosexual Men. II. Sexual Practices

J.J. Goedert, R.J. Biggar, D.M. Winn, D.L. Mann, D.P. Byar, D.M. Strong, R.A. DiGioia, R.J. Grossman, W.C. Sanchez, R.G. Kase, et al. Am J Epidemiol 1985 May;121(5):637-44.

In June 1982, the sexual practices of 245 homosexual male outpatients of private physicians were evaluated in relationship to decreased numbers of helper T lymphocytes, an abnormality that is characteristic of the acquired immunodeficiency syndrome (AIDS). Three risk groups were defined a priori—85 high-risk men from central Manhattan ("New York"), 96 intermediate-risk men from Washington, DC, with AIDS-area homosexual contacts ("Washington-exposed"), and 64 low-risk Washington, DC, men without such contacts ("Washington-unexposed"). An increasing number of homosexual partners was correlated with decreasing helper T-cell counts (R = -0.29, p = 0.009) and decreasing helpersuppressor T-cell ratios (R = -0.32, p = 0.005) in the entire study group combined and in New York subjects separately. Suppressor T-cell counts were unrelated to the number of partners in all three groups. Increasingly frequent receptive anal intercourse correlated with decreasing helper T-cell counts most clearly in the New York City group (R = -0.23, p = 0.04), somewhat less so in the Washington-exposed group (R = -0.18, p = 0.07), and not at all in the Washington-unexposed group (R = -0.09, p = 0.48). This association persisted in the New York and Washington-exposed groups after adjusting for seven other sexual practices, the number of homosexual partners, and five other potentially confounding variables. A transmissible agent associated with receptive anal intercourse best explains these data. The cause of these low helper T-cell counts may also be the cause of AIDS.

Psychosocial Factors in Admitting to Homosexuality in Sexually Transmitted Disease Clinics

M.W. Ross. Sex Transm Dis 1985 Apr-Jun;12(2):83-7.

This study investigated the factors that predict nonadmission of homosexual orientation in public and private clinics for sexually transmitted diseases in Sweden, Finland, Ireland, and Australia. Results from 604 respondents indicate that nonadmitters in all four countries are likely to conceal their orientation from most people, to expect the most negative reaction to their homosexuality, to believe in more conservative sex roles for males and females, to report themselves as more bisexual, to have had no previous sexually transmitted infections, and to have had worse relationships with their mother during adolescence than admitters. Men who attend private clinics are usually older, more conservative, of higher social class, and have had more negative reactions to their homosexuality from others. These data suggest that nonadmitters are most likely to be reassured by empathy and, particularly, explicit discussion of and expressed acceptance of homosexuality and bisexuality, reiteration of confidentiality, and avoidance of questions that assume the sex of partner. Thus, manipulation of the clinic environment may help to decrease the number of individuals who do not admit to sexual contacts with members of the same sex.

Exposure to Human T-Lymphotropic Virus Type III/Lymphadenopathy-Associated Virus and Immunologic Abnormalities in Asymptomatic Homosexual Men

J.K. Nicholson, J.S. McDougal, H.W. Jaffe, T.J. Spira, M.S. Kennedy, B.M. Jones, W.W. Darrow, M. Morgan and M. Hubbard. Ann Intern Med 1985 Jul;103(1):37-42.

Immunologic and serologic studies were done in 120 homosexual men who reportedly had no symptoms related to the acquired immunodeficiency syndrome. Forty-nine men (41%) had antibody to the retrovirus human T-lymphotropic virus type III/lymphadenopathy-associated virus (HTLV-III/LAV), and 37 (31%) had an abnormal T-cell subset ratio and other immunologic abnormalities. These abnormalities were almost exclusively confined to men seropositive for the retrovirus. Multivariate statistical analysis showed that exposure to HTLV-III/LAV was the single best predictor of T-cell (and other) immunologic abnormalities. Sexual practice, particularly receptive anal intercourse, predicted exposure to HTLV-III/LAV but was not independently related to T-cell abnormalities. The association of other microbial serologic findings with HTLV-III/LAV seropositivity or T-cell changes was a coincidental function of sexual activity. Immunologic abnormalities in asymptomatic homosexual men are mostly related to exposure to HTLV-III/LAV.

NIH Conference. The Acquired Immunodeficiency Syndrome: An Update

A.S. Fauci, H. Masur, E.P. Gelmann, P.D. Markham, B.H. Hahn and H.C. Lane. Ann Intern Med 1985 Jun;102(6):800-13.

The acquired immunodeficiency syndrome continues to be a major public health problem in the United States, and recently its spread worldwide has accelerated. The syndrome is caused by a human retrovirus transmitted by sexual contact and via blood or blood products. The virus has been isolated, characterized, and cloned, and in addition to its presence in blood, it has been found in body tissues and fluids including brain, semen, and saliva. Although the syndrome in the United States is still largely confined to male homosexuals and intravenous drug users, there is increasing evidence, particularly from Zaire, that the virus can be spread by heterosexual contact. Attempts at immune reconstitution with lymphocytes and lymphokines have resulted in some transient improvement in immune function but without clinical effect, indicating the need for specific anti-retroviral therapy in combination with immune reconstitution.

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Genital Cytomegalovirus Infection

Clinical

Epidemiology of Infections with Cytomegalovirus (CMV) and Herpes Simplex Virus in Promiscuous Women: Absence of Exogenous Reinfection with CMV

P. Wertheim, J. Galama, J. Geelen, C. Buurman and J. van der Noordaa. Genitourin Med 1985 Dec;61(6): 383-6.

Herpes simplex virus (HSV) was shed from the genital tracts of 26 (15%) and cytomegalovirus (CMV) from 19 (11%) of 177 promiscuous women. Virus excretion was especially common (HSV 41% and CMV 19%) in the youngest age group (aged 19 or less). Episodic shedding of CMV was studied by restriction enzyme analysis of the viral DNAs prepared from repeat isolates. Repeat isolates from each woman were identical, which indicated that recurrent shedding of CMV resulted from endogenous reinfection. Even under conditions of high exposure no exogenous reinfection with CMV could be shown, which indicated that exogenous reinfection is rare.

Association of Cytomegalovirus and Herpes Simplex Virus Infections of the Cervix in Four Clinic Populations

J.A. Embil, J.B. Garner, L.H. Pereira, F.M. White and F.R. Manuel. Sex Transm Dis 1985 Oct-Dec:12(4): 224-8.

The rates of isolation of cervical cytomegalovirus (CMV) and herpes simplex virus (HSV) were compared for populations of four different clinics attended by a total of 1,755 women. The prevalence of CMV infection could be predicted by the prevalence of HSV infection, with CMV being 2.5 times as prevalent as HSV in each population. The overall infection rates for CMV and HSV were 4.1 percent and 1.7 percent, respectively. The 252 women attending the Sexually Transmitted Disease Clinic had significantly higher rates of CMV and HSV infection (12.5% and 5.6%, respectively) than populations attending the other clinics. A strong relationship between marital status and CMV infection was observed. The estimated relative risk for single compared to married women was 2.9. These data verify the importance of the sexual route of transmission in the epidemiology of cervical infection with CMV.

The Incidence of Cytomegalic Inclusion Disease (CID) in an Obstetric Teaching Hospital, 1975-1984

L.I. Hatherley. Aust NZ J Obstet Gynaecol 1985 Aug;25(3):171-5.

A low incidence (1 in 4,000) of neonatal CID was found in 47,320 consecutive live births at an obstetric hospital over a decade. The mortality was high, five of 16 neonates died in the hospital and, of those discharged, seven were left with severe cerebral and/or ophthalmic handicaps. Minor, remediable conditions were also found in seven infants. Previous studies have indicated that CMV infection occurs in 1-2 percent of all pregnancies and 10 percent of the infected neonates have signs of CID at birth. A highly significant increase in the incidence of antenatal complications was found in mothers delivered of cytomegalovirus (CMV)-infected infants which may have compounded the effects of the viral disease on the fetus. A CMV-specific defect in the maternal and neonatal immune systems is discussed.

The Demographic Characteristics of Pregnant Women Infected with Cytomegalovirus

P. Griffiths, C. Baboonian and D. Ashby. Int J Epidemiol 1985 Sep;14(3):447-52.

An analysis was made of the demographic characteristics of 1,000 women who were screened for serological evidence of cytomegalovirus (CMV) infection while receiving antenatal care in central London. The prevalence of antibodies against CMV was shown, by multiple discriminant analysis, to be significantly associated with non-Caucasian race (p less than 0.001), increasing maternal age (p less than 0.001) and poor social class (p less than

0.05). These results are interpreted as reflecting increased childhood exposure to CMV as a result of poor social environments. When data from 48 women who acquired primary CMV during pregnancy were analyzed, infection was also related to non-Caucasian race (p less than 0.01), but in contrast, there was no demonstrable effect of social class, maternal age or marital status. We conclude that pregnant women acquiring the form of CMV infection with the greatest pathological potential for the fetus (primary infection) belong primarily to the middle-class sections of communities. Since middle-class women traditionally avail themselves of prophylactic measures, this result provides some optimism for the ultimate control of this common disease by immunization.

Cell-Mediated Immune Responses to Cytomegalovirus in Patients with Dysplasia of the Uterine Cervix

W.A. Neill and M. Norval. Gynecol Obstet Invest 1985;20(2):96-102.

Peripheral blood lymphocytes from 172 women with various degrees of cervical dysplasia were assayed for responsiveness to cytomegalovirus-induced early and late antigens using lymphocyte stimulation tests. No evidence was found to suggest that any group of patients was specifically sensitized to either of the antigens tested. Neither was there any difference between the patient groups in respect of mitogen-induced stimulation. The concept that cytomegalovirus might be involved in cervical cell transformation leading to carcinoma has therefore not been strengthened as a result of this study.

Cytomegalovirus Infection in Sex Partners: Evidence for Sexual Transmission

H.H. Handsfield, S.H. Chandler, V.A. Caine, J.D. Meyers, L. Corey, E. Medeiros and J.K. McDougall. J Infect Dis 1985 Feb;151(2):344-8

To examine the hypothesis that cytomegalovirus (CMV) is sexually transmitted, we determined the prevalences of antibody to CMV and viral shedding in 63 male sex partners of women with or without CMV infection, and CMV isolates from infected couples were compared by DNA restriction enzyme analysis. The prevalence of seropositivity by enzyme-linked immunosorbent assay was 31 (74%) of 42 men whose female partners were seropositive compared with five (31%) of 16 men whose partners were seronegative (P = .008). CMV was isolated from the semen or urine of four (22%) of 18 men whose female partners shed CMV from the cervix or urine compared with none of 42 whose partners were culture negative (P = .013). DNA restriction enzyme typing of CMV isolates from three pairs of sex partners showed that two of the couples were infected with common strains; epidemiologically unrelated isolates gave distinct patterns. Heterosexual contact is a major mode of transmission of CMV among some young adults.

Congenital Cytomegalovirus Infection

P.M. Preece, K.N. Pearl and C.S. Peckham. Arch Dis Child 1984 Dec;59(12):1120-6

Clinical details of 50 infants with congenital cytomegalovirus infection identified in a prospective study are reported. The mean birthweight, gestational age, and head circumference of children with congenital cytomegalovirus infection were not significantly different from those of controls. Three (6%) had symptoms at birth—two neurological and one pneumonitis. In the first four months of life, transient hepatosplenomegaly occurred in two infected children and six suffered interstitial pneumonitis. Three congenitally infected children have major neurological handicaps including spastic quadriplegia, microcephaly, and psychomotor delay, and five (10%), including the one with quadriplegia, have sensorineural deafness which is bilateral in three (6%). Estimates based on these findings suggest that the impact of congenital cytomegalovirus infection is comparable to that of congenital rubella in the era before vaccination. Of the 42 children where the nature of maternal infection was classifiable, congenital infection followed primary maternal infection in 32 (76%) and recurrent infection in 10 (24%). Neurological defects followed exposure to primary maternal infection in all three trimesters of pregnancy and also recurrent maternal infection.

Increased Prevalence of Cytomegalovirus Antibodies in Homosexual Men with Syphilis: Relation to Sexual Behavior

P. Kryger, J. Gerstoft, N.S. Pedersen and J.O. Nielsen. Scand J Infect Dis 1984;16(4):381-4.

Serum samples from 146 homosexual males, 40 heterosexual males and 51 females with at least one episode of syphilis were tested for the presence of IgG and IgM antibodies against cytomegalovirus (CMV IgG and CMV IgM). One hundred blood donors served as a control group. CMV IgG was present in 95 percent of homosexual men compared with 68 percent of heterosexual men (p less than 0.001) and 73 percent of females (p less than 0.001) with past or present syphilis. CMV IgM was found in 43-68 percent of the venereal patients and with the highest percentage in homosexual men. Only 7 percent of blood donors had CMV IgM. It is concluded that CMV infection may be regarded as a venereal disease.

Cytomegalovirus Infection in the Normal Host

J.I. Cohen and G.R. Corey. Medicine (Baltimore) 1985 Mar;64(2):100-14.

CMV mononucleosis often resembles EBV infectious mononucleosis; however, certain features of the history and physical may help to distinguish CMV from EBV. While CMV mononucleosis is usually self-limited, certain laboratory abnormalities may persist for months or years after the patient has recovered. Previous reports on CMV in the non-immunocompromised host have rarely described systemic complications. We have reviewed 10 cases of CMV with systemic manifestations at one institution over a 15-year period. These patients had prolonged fevers (often greater than three weeks) and the diagnosis was often unsuspected during the early part of the illness. While two patients required mechanical ventilation, all patients had self-limiting disease and survived. When CMV is suspected and diagnosed early in the course, numerous diagnostic (and potentially dangerous) tests can be avoided in a viral illness in which prolonged fever is common.

Laboratory Diagnosis

Immunoglobulin M Antibodies Detected by Enzyme-Linked Immunosorbent Assay and Radioimmunoassay in the Diagnosis of Cytomegalovirus Infections in Pregnant Women and Newborn Infants

S. Stagno, M.K. Tinker, C. Elrod, D.A. Fuccillo, G. Cloud and A.J. O'Beirne. J Clin Microbiol 1985 Jun;21(6):930-5.

Immunoglobulin M (IgM) antibodies were detected by a commercially available enzyme-linked immunosorbent assay (ELISA) in 36 of 49 (73%) pregnant women with primary cytomegalovirus (CMV) infection. A positive ELISA-IgM result occurred in 10 of 13 patients (77%) assessed within 8 weeks of seroconversion. The sensitivity of the radioimmunoassay (RIA) to identify primary infection in pregnant women was comparable, 78 percent in general and 86 percent for women tested within 16 weeks of seroconversion. Of the 36 women with primary infection who had detectable IgM antibodies by ELISA, 25 (69%) were delivered of congenitally infected infants, whereas of the 13 with undetectable IgM antibodies, seven (54%) transmitted the infection in utero. IgM antibodies were detected by ELISA in only five of 43 (11%) women who experienced a recurrence of CMV which either did or did not result in congenital infection. RIA was less likely to measure CMV-specific IgM in recurrent infection, inasmuch as one of 19 (5.2%) women with proven recurrent infection had detectable IgM antibody, giving RIA a better specificity for primary infection. Specific IgM antibodies were detected by ELISA in 42 of 61 (69%) babies congenitally infected with CMV and in four of 70 (5.7%) uninfected control newborn infants. The RIA was superior for diagnosis of congenital CMV infection, with a sensitivity of 89 percent and a specificity of 100 percent. The lower sensitivity of the ELISA-IgM occurred in the category of congenitally infected infants born to mothers with recurrent infection (43%), a group that is at the lowest risk of disease or to develop sequelae. This commercially available ELISA-IgM could be used in combination with a CMV-specific IgG test for monitoring women during pregnancy for primary infection.

Detection of Cytomegaloviremia Using Monoclonal Antibodies

M.C. Mazeron, R. Colimon, A. Roseto and Y. Perol. Dev Biol Stand 1984;57:287-91.

Isolation of cytomegalovirus (CMV) from blood plated on embryonic fibroblasts necessitates a delay of 10-30 days. Using monoclonal antibodies (McAb) we have developed a 96 hour test to diagnose viremia. We produced monoclonal antibodies directed against CMV (strain AD 169). Clone E 13 McAb detected a CMV early antigen in nuclei using indirect immunofluorescence. These monoclonal antibodies recognized reference strains (Davis and Towne) and 20 field isolates of CMV. E 13 McAb were, therefore, selected for the diagnostic tests. MRC 5 cells grown on coverslips in tubes were inoculated with buffy-coat from 51 blood samples from bone marrow allograft recipients and Guillain Barre polyneuritis, and centrifuged on hour at 4000 g at 36 degrees C. The indirect immunofluorescence test (IIF) was performed using E 13 McAb, 48 and 96 hours post infection. Three viremia were detected within 48 hours and five others within 96 hours. Plasma and buffy-coat were also inoculated onto MRC 5 cells grown in flasks. Flasks were observed daily for CMV cytopathic effect (CPE). CPE appeared within an average of 14 days. When CMV was detected by CPE, the IF tests were always positive within 96 hours after drawing the blood.

Comparison of a Latex Agglutination Test with Five Other Methods for Determining the Presence of Antibody against Cytomegalovirus

D.G. Beckwith, D.C. Halstead, K. Alpaugh, A. Schweder, D.A. Blount-Fronefield and K. Toth. J Clin Microbiol 1985 Mar;21(3):328-31.

A latex agglutination test for determination of antibody against cytomegalovirus was compared with five other methods: a solid-phase fluorescent immunoassay, an indirect hemagglutination test, two solid-phase enzyme immunoassays, and an indirect fluorescent-antibody method, with sera collected from 210 random blood donors. Of the sera tested, 28 percent were positive for anti-cytomegalovirus by concordance of four or more methods. The latex agglutination test performed well, with a sensitivity of 100 percent, a specificity of 99 percent, and positive and negative predictive values of 97 and 100 percent, respectively. The methods were also evaluated for the number of sera requiring repeat testing, equivocal results after retesting, ease of performance, turnaround time, and technical demands. The tests which best met the requirements for a screening test were the solid-phase fluorescent immunoassay, the indirect hemagglutination test, and the latex agglutination test. The latex agglutination test is a valuable screening tool for detecting total anti-cytomegalovirus which has high sensitivity, high negative predictive value, and rare equivocal results and also has the added advantages of ease of performance and rapid turnaround time.

Cytomegalovirus in Urine: Detection of Viral DNA by Sandwich Hybridization

M. Virtanen, A.C. Syvanen, J. Oram, H. Soderlund and M. Ranki. J Clin Microbiol 1984 Dec;20(6):1083-8

A cytomegalovirus (CMV)-specific sandwich hybridization test was constructed by using two adjacent BamHI DNA fragments of CMV DNA as reagents. The fragments were cloned into two different vectors. One of the recombinants was attached to the filter, and the other was the labeled probe. When present in the sample, CMV DNA mediated labeling of the filter by hybridizing to both the filter-bound DNA and the probe. The sandwich hybridization test was applied for the detection of CMV DNA from urine. DNA was released from virus by 2 percent Sarkosyl, concentrated by 2-butanol extraction and isopropanol precipitation, denatured, and finally subjected to the sandwich hybridization test. As a result, 70 to 90 percent of the original viral DNA could be recovered and demonstrated by the quantitative hybridization reaction. Urine could be stored at room temperature in Sarkosyl for at least 2 days without affecting the detectability of CMV. The clinical applicability of the test was evaluated by studying urine samples from four infants excreting CMV. Sandwich hybridization demonstrated the presence of CMV DNA in all of the specimens. These contained originally 10(5) to 10(8) CMV DNA molecules per ml.

Therapy

Prevention and Treatment of Cytomegalovirus Infections with Interferons and Immune Globulins

J.D. Meyers. Infection 1985;13 Suppl 2:S211-8.

With the exception of congenitally-infected infants, cytomegalovirus infection is generally benign in persons with normal host defenses. In contrast, among immunosuppressed patients, these infections may be severe and sometimes fatal. Treatment of cytomegalovirus infection with presently available antiviral agents including interferons has not been successful. Prevention of infection has been successful in several circumstances, however. Cytomegalovirus is transmitted by blood products from seropositive donors, and screening to remove seropositive blood products or freezing to destroy leukocytes has been effective amont neonates, cardiac transplant patients, and renal dialysis patients. An alternative approach used among marrow transplant patients is passive immunization of seronegative patients with plasma or globulins with high antibody titers against cytomegalovirus. Alpha interferon given prophylactically has been effective in delaying virus reactivation and reducing the severity of infection among seropositive renal transplant patients. All of these approaches, as well as the continued development of more effective antiviral agents, will be needed for control of cytomegalovirus infection.

Research and Evaluation

Acquisition of Cytomegaloviral Infections in Families with Young Children: A Serological Study

L.H. Taber, A.L. Frank, M.D. Yow and A. Bagley. J Infect Dis 1985 May;151(5):948-52.

Acquisition of cytomegalovirus (CMV) infection in families with young children was investigated with serial serological tests for antibody to CMV by using ELISA and anti-complement immunofluorescence. Members of 68 Houston families were studied for a mean of 3.5 years. Seroconversion occurred in one or more members of 37 (53%) of 68 families studied. The mean annual seroconversion rate was 10 percent for fathers, 10.6 percent for mothers, and 10.3 percent for children. The attack rate for susceptible family members (including the index case) was 54 percent. The index case was the child in 10 instances, the father in 2, and the mother in 2. The index case could not be identified in 23 families. This Houston study indicates that the family with young children is a high-risk setting for CMV infection. This is an important concern regarding risks for mothers in their childbearing and child-rearing years.

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*Abstracted

Syphilis

Clinical

Acute Syphilitic Meningitis. Its Occurrence after Clinical and Serologic Cure of Secondary Syphilis with Penicillin G

L.L. Bayne, J.W. Schmidley and D.S. Goodin. Arch Neurol 1986 Feb;43(2):137-8.

Acute syphilitic meningitis developed in a 36-year-old man three months after apparently successful treatment of secondary syphilis with doses of penicillin G benzathine recommended by the current Centers for Disease Control guidelines. He was then treated with high-dose intravenous penicillin G sodium, with resolution of symptoms and cerebrospinal fluid abnormalities. Although other instances of neurosyphilis following adequate therapy for early syphilis have been reported, in most cases reinfection cannot be convincingly excluded. We believe this patient represents a particularly well-documented example of progression to neurosyphilis, despite recommended therapy with penicillin. A review of recently reported cases suggests that progression of syphilis, despite "appropriate" therapy, is not an isolated event.

Syphilis Tests in Diagnostic and Therapeutic Decision Making

G. Hart. Ann Intern Med 1986 Mar;104(3):368-76.

Predictive value calculations were used to derive diagnostic guidelines for syphilis. Specificity of the VDRL (Venereal Disease Research Laboratory) and treponemal tests is high in healthy persons but less in elderly and ill persons. Sensitivity of the VDRL test is high in secondary and early latent syphilis but reduced in primary and late syphilis or in cerebrospinal fluid evaluations. Primary syphilis should be diagnosed by darkfield microscopy, with VDRL confirmation for atypical lesions. Screening of asymptomatic persons with the VDRL test, followed by treponemal test confirmation on positive sera, is recommended for all pregnant women, contacts of persons with infectious syphilis, and other high-risk groups. Quantitative VDRL assessment at 3, 6, and 12 months after treatment should be used to assess the adequacy of treatment for both late latent and early syphilis. Cerebrospinal fluid VDRL assessment and cell count should be restricted to seropositive persons with a high risk of neurosyphilis.

Tonic Pupils in Neurosyphilis

W.A. Fletcher and J.A. Sharpe. Neurology 1986 Feb;36(2):188-92.

Of 60 patients with tonic pupils, 29 had serologic tests for syphilis. Five patients had positive blood serology and confirmatory tests; four had other manifestations of neurosyphilis and positive CSF serology. All seropositive patients had bilateral tonic pupils with light-near dissociation and denervation hypersensitivity. Of the ten tonic pupils, only one was miotic and one dilated. Although tonic pupils tend to become small and bilateral, they should be distinguished readily from Argyll Robertson pupils, which react briskly, not tonically, to near stimuli. Patients with bilateral tonic pupils should have serologic tests for syphilis.

Characterization of the Antigenic Determinants and Host Components in Immune Complexes from Patients with Secondary Syphilis

R.E. Baughn, M.C. McNeely, J.L. Jorizzo and D.M. Musher. J Immunol 1986 Feb 15;136(4):1406-14.

Sera from patients with secondary syphilis were evaluated for abnormal levels of circulating immune complexes (IC), immunoglobulins (Ig), and complement components. Clq-solid-phase assays (Clq-SPA) that made use of monoclonal and polyclonal antibodies directed against IgG subclasses indicated that human IC were composed primarily of IgG3 and IgG1; these findings appeared consistent with subclass profile responses of electrophoretically transferred blots (Western blots) of *Treponema pallidum* reacted with syphilitic sera. Complexes were isolated from reactive sera by polyethylene glycol precipitation followed by either anti-Clq column chromatography or protein A-Sepharose chromatography. Although qualitative and quantitative differences were noted, all purified materials contained a treponemal polypeptide antigen with a m.w. of approximately 87,000. Subsequent analysis of this polypeptide, which was also present in purified IC from rabbits with experimental syphilis, suggests that it may represent the fibronectin receptor of the organism. The 76,000 and 66,000 materials, earlier identified in purified rabbit IC, appeared to represent C-terminal degradation products of fibronectin presumably of host origin, rather than treponemal antigens. Although fibronectin binds avidly to Clq and could represent a co-precipitable contaminant throughout the isolation procedure, anti-fibronectin antibodies in the sera of patients detectable by radioimmunoassay and the present of antibodies to 76,000 and 66,000 dalton fibronectin fragments in the globulin fractions of disassociated complexes argues against such a conclusion.

Solitary Oral Condylomata Lata in a Patient with Secondary Syphilis

B. de Swaan, K.H. Tjiam, V.D. Vuzevski, T. Van Joost and E. Stolz. Sex Transm Dis 1985 Oct-Dec; 12(4):238-40.

A case report of a patient with oral condylomata lata is presented. Physical examination showed that the lesions were the only symptom of secondary syphilis. The diagnosis was based on darkfield microscopy of specimens from the lesions and serologic tests for syphilis. The condylomata lata responded well to treatment of the syphilis with procaine penicillin G.

Meningovascular Syphilis: CT and MR Findings

B.A. Holland, L.V. Perrett and C.M. Mills. Radiology 1986 Feb;158(2):439-42.

The radiologic findings in three cases of meningovascular syphilis are presented. Angiography demonstrated varying degrees of narrowing and ectasia of the supraclinoid carotid, basilar, and proximal anterior and middle cerebral arteries, as well as distal branches. Computed tomography (CT) showed multifocal infarction with variable enhancement. Similarly, in the one case studied with magnetic resonance (MR), several regions of high signal intensity on T2-weighted sequences were found, which were compatible with foci of ischemia. Although the radiologic findings are nonspecific, the diagnosis of meningovascular syphilis should be considered in patients with vasculitis of uncertain etiology.

Extragenital Syphilitic Chancres

T.A. Chapel, P. Prasad, J. Chapel and N. Lekas. J Am Acad Dermatol 1985 Oct;13(4):582-4.

Two patients with extragenital chancres are presented to emphasize unusual expressions of primary syphilis. The clinical presentations and differential diagnosis of extragenital chancres are discussed.

Multiple Neuropathic Arthropathy in a Patient with Syphilis

B. Fishel, M. Dan, M. Yedwab, M. Yaron and S. Shibolet. Clin Rheumatol 1985 Sep;4(3):348-52.

An unusual case of neuropathic arthropathy in a patient with tabes dorsalis is presented. The special feature consisted of multiple joint involvement in the upper limbs and spine. This uncommon location of Charcot joints can probably be attributed to the patient's occupation which involved heavy strains on his upper limbs.

An Unusual Presentation of Oral Syphilis

S.D. Jefferies and R.A. Ord. Br J Oral Maxillofac Surg 1985 Oct;23(5):376-80.

A case of late, non-infectious, gummatous syphilis presenting with intra-oral arterial hemorrhage in an 81 year-old lady is described.

Arsenic, Syphilis, and Cancer of the Prostate

R.E. Lees, R. Steele and D. Wardle. J Epidemiol Community Health 1985 Sep;39(3):227-30.

A study was conducted to investigate the association of cancer of the prostate with historical records of previous venereal disease and treatment with arsenical drugs. Eighty-three cancer cases were each age matched with two male controls—one with benign prostatic hypertrophy and one other non-cancer patient. Analysis from pooled data showed a statistically significant difference for syphilis infection between cases and controls at p less than 0.05; odds ratio 2.9. Matched pair analysis maintained p less than 0.05 significance for the first control group, but odds ratios were 5.5 and 2.75 in respect of control groups 1 and 2. The mean age at which venereal infection was acquired was higher for syphilis than for gonorrhea, but the mean age at diagnosis of cancer was younger for the syphilis group; there was a statistically significant difference between the mean at cancer diagnosis of those who had syphilis and those who had no record of previous venereal infection ($t = 2.18$, df 70, p less than 0.05). No association was demonstrated for history of treatment with arsenical drugs.

Serological Response to Syphilis Treatment. A New Analysis of Old Data

S.T. Brown, A. Zaidi, S.A. Larsen and G.H. Reynolds. JAMA 1985 Mar 1;253(9):1296-9

One important aspect of the posttreatment evaluation of patients with early syphilis is assessment of serological test results. Using information previously collected from 818 patients in the Early Syphilis Study, we evaluated the seroresponse of people treated for primary or secondary syphilis. We generated curves describing the VDRL titer declines with time. The VDRL titer declined approximately fourfold at three months and eightfold at six months. These observations will allow clinicians to identify treatment failures or reinfections at the earliest possible time during their follow-up.

Neurosyphilis in the Antibiotic Era

J.M. Burke and D.R. Schaberg. Neurology 1985 Sep;35(9):1368-71.

Among 30 patients with neurosyphilis diagnosed between 1970 and 1981, 43 percent had symptoms attributable to neurosyphilis, 43 percent had unrelated symptoms, and 14 percent were asymptomatic. Serum VDRL was positive in 86 percent, and the CSF VDRL was positive in 53 percent. Meningovascular and vascular syphilis were relatively more common than in the prepenicillin era; tabes dorsalis and general paresis were unchanged in relative frequency.

The Human Respiratory Nasal Mucosa in Nasal Syphilis. An Ultra-Microscopic Study

H. Toppozada, M. Talaat and S. Elwany. Acta Otolaryngol (Stockh) 1985 Mar-Apr;99(3-4):272-9.

The fine structure of the human tertiary syphilitic nasal mucosa was studied in five patients. The epithelium showed variations in thickness, loss of cilia, irregular cell contours, widened intercellular spaces, rare goblet cells. The seromucinous glands were in three forms. The arterioles and capillaries varied in relation to the pathology of the surrounding tissue. The venules were least affected. The stroma was infiltrated by macrophages, plasma cells with some areas having excessive fibrosis and others partially necrotic. These findings were correlated to the histochemical reactions. Scattered *Treponema pallidum* were seen, demonstrating the blood-borne dissemination and the infective nasal secretions.

Congenital Syphilis Revisited

L. Mascola, R. Pelosi, J.H. Blount, C.E. Alexander and W. Cates, Jr. Am J Dis Child 1985 Jun;139(6):575-80.

Despite decades of experience with congenital syphilis, problems still arise in case definition, diagnostic evaluation, treatment, and follow-up. We reviewed all 50 cases of early congenital syphilis reported to the State of Texas in 1982. A large proportion of the infants were premature (39%), of low birth weight (38%), and symptomatic at birth (62%). Because of these findings, we believe that possible cases of asymptomatic congenital syphilis in Texas may be under-reported. Laboratory and/or roentgenographic findings were important to confirm the diagnosis of congenital syphiiis. Over half of the asymptomatic infants had positive results of cerebrospinal fluid VDRLs. After diagnosis, the treatment of infants with penicillin varied considerably. While all 47 living infants were treated with penicillin, 21 different regimens were used. We urge all physicians to perform complete diagnostic evaluations on suspected infants consisting of a quantitative serum test for syphilis, serum IgM levels, a cerebrospinal fluid VDRL, roentgenographs of the long bones, and dark-field microscopy where indicated. Additionally, infants and their families need appropriate follow-up after treatment.

Lumbar Puncture in Asymptomatic Late Syphilis. An Analysis of the Benefits and Risks

J. Wiesel, D.N. Rose, A.L. Silver, H.S. Sacks and R.H. Bernstein. Arch Intern Med 1985 Mar;145(3):465-8.

We evaluated the treatment of asymptomatic patients with untreated syphilis of more than one year's duration (asymptomatic late syphilis) using a decision-analysis model. Two strategies were compared: treatment with 7.2 million units of penicillin G benzathine, or performing a lumbar puncture to test for asymptomatic neurosyphilis followed by penicillin and management based on cerebrospinal fluid analysis. Estimates of probabilities of disease prevalence, test sensitivity, and cure and complication rates were derived from published studies. Both strategies resulted in a cure rate of at least 99.7 percent using the best estimates. Although the strategy using lumbar puncture results in a 0.2 percent higher cure rate, its rate of complications (0.3%) exceeds its marginal benefit. We conclude that a lumbar puncture offers little additional benefit and may increase morbidity in patients with asymptomatic late syphilis.

Skeletal Presentation of Congenital Syphilis: Case Report and Review of the Literature

J.S. Toohey. J Pediatr Orthop 1985 Jan-Feb;5(1):104-6.

Congenital syphilis is a rare disease. Primary skeletal presentation is also unusual, and recognition and prompt treatment are necessary to avoid devastating consequences. Differential diagnoses include trauma, Caffey's disease, scurvy, and hypervitaminosis D. Penicillin treatment will reverse most changes.

Miliary Pustular Syphilid

G.D. Waldman and R.D. Wise. Cutis 1984 Dec;34(6):556-8.

A case of secondary syphilis is presented in which a dramatic generalized eruption of pustules and an elevated temperature were prominent features. Biopsy of the skin lesions showed dermal granulomata, which are occasionally seen in the papulopustular lesions of secondary syphilis. The classification of pustular syphilids is reviewed.

Laboratory Diagnosis

Inappropriate Use of the Cerebrospinal Fluid Venereal Disease Research Laboratory (VDRL) Test to Exclude Neurosyphilis

P.E. Dans, L. Cafferty, S.E. Otter and R.J. Johnson. Ann Intern Med 1986 Jan;104(1):86-9.

Only three of 2,536 cerebrospinal fluid (CSF) VDRL tests ordered at the Johns Hopkins Hospital in 1980 were positive. Of patients on whom the test was ordered, 226 had a positive or borderline serum fluorescent treponemal antibody absorption test. Records from 156 (69%) of these patients, including all three with positive CSF-VDRL tests, were reviewed and showed that the diagnosis of neurosyphilis had been considered only in 44 (28%). One-third of records lacked notations of historical and physical findings characteristic of neurosyphilis. Forty seropositive patients who had lumbar puncture to rule out asymptomatic neurosyphilis had negative CSF-VDRL tests; none had neurosyphilis diagnosed. Use of the CSF-VDRL test seemed to represent predominantly "box-checking" on the requisition to rule out neurosyphilis. Yet the test performs better when "ruling in" rather than ruling out neurosyphilis. The Centers for Disease Control should reevaluate its recommendation to rule out neurosyphilis in asymptomatic patients with untreated syphilis of greater than 1 year's duration, given the costs, risks, and dubious benefits.

Antigens of *Treponema pallidum* Recognized by IgG and IgM Antibodies During Syphilis in Humans

S.A. Baker-Zander, E.W. Hook, III, P. Bonin, H.H. Handsfield and S.A. Lukehart. J Infect Dis 1985 Feb;151(2):264-72

IgG and IgM antibody specificities for antigens of *Treponema pallidum* Nichols strain were determined by using sodium dodecyl sulfate-polyacrylamide gel electrophoresis and the western blot technique in sera from patients with untreated syphilis, normal persons, persons with biologic false-positive tests for syphilis, and sexual contacts of persons with infectious syphilis. IgG reactivities of sera from individuals with primary syphilis varied considerably but consistently exhibited strong reactivity to a 48-kilodalton band. Sera from patients with secondary and early latent syphilis uniformly demonstrated reactivity to 22 separate polypeptide antigens; decreased reactivity was seen in late latent syphilis. Normal and biologic false-positive sera showed weak IgG reactivity against none to 12 polypeptides. Sera from asymptomatic contacts of persons with infectious syphilis showed reactivity to a varying number of treponemal antigens, including some reactions not seen with normal sera. IgM reactivity was most prominent in secondary syphilis but was demonstrable at all stages of disease.

Double-Conjugate Enzyme-Linked Immunosorbent Assay for Immunoglobulins G and M Against *Treponema pallidum*

C.E. Farshy, E.F. Hunter, S.A. Larsen and E.H. Cerny. J Clin Microbiol 1984 Dec;20(6):1109-13

An enzyme-linked immunosorbent assay (ELISA) for the simultaneous measurement of immunoglobulin G (IgG) and IgM was developed to detect antibodies to *Treponema pallidum*. Wells of polystyrene microtiter plates were coated with *T. pallidum* antigen, diluted patient serum was added, and IgG and IgM which bound to the *T. pallidum* antigen were measured by the simultaneous addition of alkaline phosphatase-labeled anti-human IgG and horseradish peroxidase-labeled anti-human IgM. Bound IgG was detected first, followed by bound IgM. After development of the procedure, 145 categorized sera were evaluated: 60 from individuals without syphilis; 62 from patients with syphilis, including 22 with primary, 20 with secondary, and 20 with latent phases of syphilis; and 23 from patients with rheumatoid arthritis. Of the 60 sera from individuals without syphilis, 100 percent were nonreactive for IgG antibody and 16 percent were reactive for IgM. Of the 23 sera from patients with rheumatoid arthritis, 3 were reactive for IgG and 3 were nonreactive for IgM. Of the 62 sera from patients with syphilis, 61 (98%) were reactive for IgG antibody with increased titers as the stage of syphilis increased, whereas IgM reactivity decreased. This enzyme-linked immunosorbent assay appears to be a simple method for the simultaneous measurement of antibodies under equal assay conditions.

Treponema pallidum Specific IgM Hemagglutination Test for Serodiagnosis of Syphilis

T. Sato, E. Kubo, M. Yokota, T. Kayashima and T. Tomizawa. Br J Vener Dis 1984 Dec;60(6):364-70

The *Treponema pallidum* specific IgM hemagglutination (TP-IgM-HA) test uses erythrocytes sensitized with antiserum to human IgM to separate IgM from IgG in serum. Specific antitreponemal IgM captured in this way is detected by adding a second reagent comprising erythrocytes sensitized with *T. pallidum* antigen. Eighty-two serum samples from 82 patients with untreated syphilis, 521 samples from 73 patients with treated syphilis, and 1,872 samples from people who did not have syphilis were examined by the 19S(IgM)-TPHA (*T. pallidum* hemagglutination), IgM-FTA-ABS (fluorescent treponemal antibody absorbed), TP-IgM-ELISA (enzyme linked immunosorbent assay), and TP-IgM-HA tests for the presence of 19S(IgM) antibodies specific to treponemes. The sensitivity of the TP-IgM-HA test was 97.6 percent and the specificity was 99.7 percent. We also traced IgM specific to treponemes in untreated patients with primary syphilis by four different tests. The TP-IgM-HA test results clearly reflected the effect of the treatment.

Therapy

Survival of Treponemes after Treatment: Comments, Clinical Conclusions, and Recommendations

E.M. Dunlop. Genitourin Med 1985 Oct;61(5):293-301.

Treponemes may persist after treatment that has been accepted as effective; the reasons for this are discussed. Nevertheless, the epidemic of syphilis after the second world war was not followed by an epidemic of late syphilis, and the results of treatment with penicillin are excellent. Neurological signs may progress in some treated patients, and the standard doses of soluble penicillin and any dose of benzathine penicillin (even with added probenecid by mouth) cannot be relied on to achieve treponemicidal concentrations in the cerebrospinal fluid (CSF). There are no large scale studies of CSF findings after treatment of early syphilis with benzathine penicillin. Standard dosage, such as procaine penicillin G 600,000 international units (IU) by intramuscular injection for 10 days, is the treatment of choice for the patient suffering from uncomplicated early syphilis; this should be preferred to benzathine penicillin, which should only be used when standard treatment as above cannot be given. Treponemicidal concentrations of penicillin should be achieved in the CSF of patients suffering from neurosyphilis by schedules of probenecid by mouth and procaine penicillin by single daily intramuscular injections; treatment should last for 17 to 21 days. Benzathine penicillin should not be used for the treatment of patients suffering from neurosyphilis or from the iritis of late syphilis including that accompanying interstitial keratitis.

Research and Evaluation

Monoclonal Antibodies to *Treponema pallidum*

H.J. van de Donk, J.D. van Embden, A. de Jong, M.F. van Olderen and A.D. Osterhaus. Dev Biol Stand 1984;57:107-11.

Three successive fusions of mouse myeloma cells and spleen lymphocytes of a mouse immunized with *Treponema pallidum* resulted in one hybridoma producing anti-*T. pallidum* antibodies for each fusion. The mice were immunized with live pallidum cells respectively 1, 3, and 5 months before fusion and with antigen purified on density gradients 4, 3, and 2 days before fusion. Hybridomas cultures were tested for antibody production with an Enzyme Linked Immunosorbent Assay (ELISA) and a Western blotting technique. Two of the three anti-*T. pallidum* antibody producing hybridomas were found with the ELISA, the third was found with a Western blotting technique. These hybridomas were also tested for the production of antibodies to rabbit antigens and *T. phagedenis* antigens in the ELISA: none appeared to be positive. Two of the hybridomas produce antibodies to a *T. pallidum* protein antigen of a molecular weight of 46 000: one hybridoma produces antibodies to a *T. pallidum* protein antigen of a molecular weight of 44,000 as determined by the Western blotting. Antibodies against these antigens are found during almost all stages of syphilis in man. One of the hybridomas produces monoclonal antibodies that react with treponemal antigen from *E. coli* cells, prepared by recombinant DNA technology as appeared in the Western blotting technique and this antibody will be used for purification of the 44,000 protein.

Oxygen Toxicity in *Treponema pallidum*: Deoxyribonucleic Acid Single-Stranded Breakage Induced by Low Doses of Hydrogen Peroxide

B.M. Steiner, G.H. Wong, P. Sutrave and S. Graves. Can J Microbiol 1984 Dec;30(12):1467-76.

The effect of hydrogen peroxide on *Treponema pallidum* was investigated. The in vitro loss of virulence (as measured by rabbit inoculation) of *T. pallidum* was accelerated by as low as 100 microM hydrogen peroxide in the complex maintenance medium used. Higher doses led to rapidly accelerated death with 500 microM hydrogen peroxide causing sterilization of the medium within 3 to 4 hours. Since hydrogen peroxide is known to cause single-stranded breaks in DNA, the effect of hydrogen peroxide on the treponemal genome was examined. Extensive breakage was caused by 100 microM hydrogen peroxide as determined on alkaline sucrose gradients. A limit was reached at 250 microM and above. Single-stranded breaks could be demonstrated as early as 5-10 minutes after exposure to hydrogen peroxide when the treponemes were exposed to 250 microM hydrogen peroxide; accelerated death was evident by 2 hours past exposure demonstrating that DNA breakage was preceding death. Treponemal death caused by penicillin did not result in DNA breakage. The repair-proficient bacterium *Escherichia coli* K-12 was compared with *T. pallidum*. It required 10-100 times more hydrogen peroxide to cause various levels of breakage. *Escherichia coli* K-12 rapidly repaired DNA breakage once hydrogen peroxide was removed by addition of catalase. *Treponema pallidum*, in comparison, showed little or no repair in vitro. Addition of catalase or dithiothreitol to the medium protected against all but a low level of breakage; this may reflect on the ability of catalase and reducing agents to protect *T. pallidum* against oxygen toxicity in vitro.

Experimental Infection of Inbred Guinea Pigs with *Treponema pallidum*: Development of Lesions and Formation of Antibodies

C.S. Pavia and C.J. Niederbuhl. Genitourin Med 1985 Apr;61(2):75-81.

Inbred strain 2 and strain 13 guinea pigs were infected intradermally in the hind legs with different numbers of the virulent Nichols strain of *Treponema pallidum*. About 91 percent of the animals developed clearly visible lesions after being injected with 5 X 10(6) to 10 X 10(6) treponemes. *T. pallidum* organisms could be isolated from skin lesions at various stages after infection. Infected animals were monitored for the production of specific treponemal and nonspecific cardiolipin antibodies by the fluorescent treponemal antibody (FTA) and microhemagglutination (MHA-TP) tests, and the rapid plasma reagin (RPR) card test. Low levels of specific antibodies could be detected by both FTA and MHA-TP tests from three to four weeks after infection. Maximum titres of treponemal antibody generally occurred after week 6 and persisted for several more months. These peak titres ranged from 1/40 to 1/80 in the FTA test and 1/160 to 1/320 in the MHA-TP test. During the same period infected guinea pigs, unlike rabbits with syphilis, did not produce detectable quantities of antibodies against cardiolipin.

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Pelvic Inflammatory Disease

Clinical

Serum C-Reactive Protein Determination in Acute Pelvic Inflammatory Disease

M. Lehtinen, S. Laine, P.K. Heinonen, K. Teisala, A. Miettinen, R. Aine, R. Punnonen, P. Gronroos and J. Paavonen. Am J Obstet Gynecol 1986 Jan;154(1):158-9.

We have studied the role of serum C-reactive protein determination in the diagnosis of acute pelvic inflammatory disease. Acute-phase serum C-reactive protein concentration reflected the extent and the severity of pelvic inflammatory disease more closely than erythrocyte sedimentation rate or white blood cell count determinations. We recommend that both C-reactive protein concentration and erythrocyte sedimentation rate should be routinely used to augment the clinical diagnosis of pelvic inflammatory disease.

Role of Aerobic Gram-Negative Bacilli in Endometritis after Cesarean Section

R.S. Gibbs, J.D. Blanco and S. Bernstein. Rev Infect Dis 1985 Nov-Dec;7 Suppl 4:S690-5.

Endometritis is considered to be a polymicrobial infection, involving aerobes, anaerobes, and genital mycoplasmas. Aerobic gram-negative rods make up 7-25 percent of all genital isolates, but findings from studies in which special collection techniques were used suggest that many of these may be contaminants from the lower genital tract. Bacteremia occurs in 4-30 percent of patients with endometritis, and aerobic gram-negative rods account for approximately 25 percent of blood isolates. Both selected therapy studies and studies of intrauterine cultures collected at surgery from patients at risk for endometritis suggest the significant role of aerobic gram-negative rods. Among them *Escherichia coli* is the most common isolate in both genital and blood cultures. *Klebsiella pneumoniae* and *Proteus mirabilis* rank next, followed by Enterobacter species. Pseudomonas species account for fewer than 0.6 percent of genital isolates. Overall, aerobic gram-negative rods are causally involved in 10-20 percent of cases of endometritis following cesarean section.

Hospitalizations among Black Women Using Contraceptives

J.E. Higgins, L.R. Wilkens, I.C. Chi and R.A. Hatcher. Am J Obstet Gynecol 1985 Oct 1:153(3):280-7.

We analyzed hospitalizations among 26,507 young black women who attended a large metropolitan family planning clinic between 1968 and 1976. Age-adjusted hospitalization rates were compared for women using oral contraceptives, intrauterine contraceptive devices, and depot medroxyprogesterone acetate. Overall, intrauterine contraceptive device and depot medroxyprogesterone acetate users were hospitalized at about the same rate, while women using oral contraceptives were hospitalized 30 percent less often. The oral contraceptive users were not hospitalized at a higher rate for circulatory disease. Compared to women using intrauterine contraceptive devices, users of oral contraceptives and depot medroxyprogesterone acetate were less likely to be hospitalized for benign breast disease (rate ratios = 0.5 and 0.2, respectively, with 95% confidence limits of 0.3 to 0.7 and 0.1 to 0.5) and for pelvic inflammatory disease. Women were four times as likely to be using depot medroxyprogesterone acetate when they were hospitalized with carcinoma in situ of the cervix, but depot medroxyprogesterone acetate users with at least 3 years of use were less likely to be hospitalized for carcinoma in situ than comparable groups of oral contraceptive and intrauterine contraceptive device users.

Introductory Address: Microbial Etiology of Pelvic Inflammatory Disease

P. Mardh. Sex Transm Dis 1984 Oct-Dec;11(4 Suppl):428-9

The etiology of acute pelvic inflammatory disease is multifactorial, and the pattern of organisms most frequently causing the condition fluctuates. For example, tuberculous salpingitis has gradually become a rarity in many areas, and cases of nongonococcal salpingitis have started to outnumber those of gonococcal salpingitis. *Chlamydia trachomatis* now causes more cases than *Neisseria gonorrhoeae* in many regions. *Mycoplasma hominis* is another (often overlooked) etiologic agent infection in the upper genital tract of women. Pelvic inflammatory disease due to anaerobic microorganisms seems to occur more frequently in some areas (i.e., the United States) than in others (i.e., Europe).

Microbiological and Histological Findings in the Fallopian Tubes of Women Using Various Contraceptive Methods

J.A. Collins, P.G. Gillett, I.A. Perlin, J.A. Embil, I. Zayid, G. Richards and M.E. Kirk. Contraception 1984 Nov;30(5):457-66

The oviducts of seventy-three women undergoing sterilization by partial salpingectomy were submitted for microbiological and histologic studies. Twenty women were intrauterine device users, twenty-five women were oral contraceptive pill users and twenty-eight women used natural or barrier methods of contraception. Among intrauterine device users, there was an excess of mild and severe acute inflammatory histologic changes involving both the lumen and the tubal mucosa. Five of the eight intrauterine device users with acute inflammatory change had sterile tubal cultures.

Infections with *Neisseria gonorrhoeae* and *Chlamydia trachomatis* in Women with Acute Salpingitis

G.B. Kristensen, A.C. Bollerup, K. Lind, P.A. Mcardh, P. Ladehoff, S. Larsen, A. Marushak, P. Rasmussen, J. Rolschau, I. Skoven, et al. Genitourin Med 1985 Jun;61(3):179-84.

The value of cultural and serological procedures in diagnosing gonococcal and chlamydial infections was investigated in 85 women who had provisional diagnoses of pelvic inflammatory disease. The correlation between certain clinical variables and the absence or presence of such infections was also studied. In 46, the diagnosis of acute salpingitis was verified by laparoscopy. The laboratory and clinical findings in the patients with acute salpingitis were compared with those in the remaining 39 women in whom laparoscopy did not show signs of inflammation. Salpingitis was considered to be gonococcal if *Neisseria gonorrhoeae* was isolated or a fourfold or more change in titre of antibodies to gonococcus pilus antigen was found. The diagnosis of chlamydial salpingitis was based on the isolation of *Chlamydia trachomatis*, a fourfold or more change in titre of IgG antibodies to or from a titre of greater than or equal to 1/256, or the presence of IgG antibodies at a titre of greater than or equal to 1/512. Patients with chlamydial salpingitis had less severe symptoms but a more protracted course of disease than patients with gonococcal salpingitis or with acute salpingitis not associated with the two pathogens.

Detection of Herpes Simplex Virus in Women with Acute Pelvic Inflammatory Disease

M. Lehtinen, I. Rantala, K. Teisala, P.K. Heinonen, T. Lehtinen, R. Aine, A. Miettinen, P. Gronroos, R. Punnonen, P. Leinikki, et al. J Infect Dis 1985 Jul;152(1):78-82.

Four women are described with acute salpingitis confirmed by laparoscopy who had herpes simplex virus (HSV) isolated from the cervix or the upper genital tract (endometrium, fallopian tube, or cul-de-sac) or both. None of the patients had overt genital herpes, but one had typical HSV cervitis on a cervicovaginal smear stained with Papanicolaou's stain, one had a significant change in level of antibodies to HSV, and one had an endometrial biopsy specimen positive for HSV antigen. There are at least three potential explanations for these findings: chronic viral shedding, viral reactivation caused by acute pelvic inflammatory disease (PID), or that the PID was actually caused by HSV. Further prospective studies are needed to document the role of HSV in causing PID.

Differential Diagnosis of Appendicitis and Pelvic Inflammatory Disease. A Prospective Analysis

F. Bongard, D.V. Landers and F. Lewis. Am J Surg 1985 Jul;150(1):90-6.

Diagnosis of the cause of lower abdominal pain in women may be difficult because appendicitis and pelvic inflammatory disease often present similarly. In a prospective study of 118 women, we found that several criteria are useful in establishing this differential. These include: (1) duration of symptoms, (2) the presence of nausea, vomiting or both, (3) a history of venereal disease, (4) cervical motion tenderness, (5) adnexal tenderness, and (6) isolated peritoneal signs in the right lower quadrant. Although no single finding can define the diagnosis, the history and physical findings reported herein provide a number of criteria which, when taken together, will usually allow a confident diagnosis of either appendicitis or pelvic inflammatory disease to be made. Attention to these items can improve precision in diagnosis and lessen the incidence of unnecessary laparotomy, which carries a well-documented complication rate of 10 to 20 percent.

Endometritis and Acute Salpingitis Associated with *Chlamydia trachomatis* and Herpes Simplex Virus Type Two

J. Paavonen, K. Teisala, P.K. Heinonen, R. Aine, A. Miettinen, M. Lehtinen and P. Gronroos. Obstet Gynecol 1985 Feb;65(2):288-91

A patient who had endometritis confirmed by endometrial biopsy and acute salpingitis confirmed by laparoscopy is reported. *Chlamydia trachomatis* and herpes simplex virus type two were isolated from the endometrial cavity and the fallopian tube. The histopathologic findings of the endometritis were similar to those frequently seen in chronic chlamydial eye disease or chlamydial cervicitis.

Pelvic Inflammatory Disease After Hysterosalpingography Associated with *Chlamydia trachomatis* and *Mycoplasma hominis*

B.R. Mller, J. Allen, B. Toft, K.B. Hansen and D. Taylor-Robinson. Br J Obstet Gynaecol 1984 Dec;91(12):1181-7

A total of 116 women were referred for hysterosalpingography because of primary or secondary infertility. *Chlamydia trachomatis* was isolated from the cervix of four (3.4%) of the patients, whereas *Mycoplasma hominis* was isolated from 39 (33.6%) of them. Four patients developed acute pelvic inflammatory disease after hysterosalpingography; two of them were chlamydia culture-positive and developed a significant chlamydial antibody response during the course of the disease. One of the other two patients, who developed upper genital-tract infection, was culture positive for *M. hominis* and developed a significant antibody response to this micro-organism. The results indicate that *C. trachomatis* should be sought in patients before hysterosalpingography and, if detected, appropriate antibiotic cover should be instituted before the procedure.

Hemophilus influenzae Causes Purulent Salpingitis

J. Paavonen, M. Lehtinen, K. Teisala, P.K. Heinonen, R. Punnonen, R. Aine, A. Miettinen and P. Gronroos. Am J Obstet Gynecol 1985 Feb 1;151(3):338-9

We describe two patients with laparoscopically diagnosed, severe acute salpingitis who had nontypable *Hemophilus influenzae* isolated directly from the fallopian tubes. Nontypable *H. influenzae* should be recognized as an important genital pathogen.

Oral Contraceptives, *Chlamydia trachomatis* Infection, and Pelvic Inflammatory Disease. A Word of Caution about Protection

A.E. Washington, S. Gove, J. Schachter and R.L. Sweet. JAMA 1985 Apr 19;253(15):2246-50.

Management of pelvic inflammatory disease (PID) and decisions about contraception are being influenced by reports that oral contraceptives decrease the risk of PID. To evaluate the validity of this association, we have examined published epidemiologic evidence and reviewed relevant information from other disciplines. Current information does not permit the generalization that oral contraceptives protect against all forms of PID. Most studies conducted (1) have been limited to hospitalized women, who represent less than 25 percent of all PID cases and are likely to have relatively severe forms of the disease, and (2) have failed to distinguish between gonococcal and nongonococcal PID. While oral contraceptives may provide some protection against gonococcal PID, no basis exists for assuming similar protection is provided against chlamydial PID. In fact, epidemiologic and biologic evidence suggests that infection with *Chlamydia trachomatis*, the leading cause of nongonococcal PID, is enhanced by oral contraceptives. We judge the conclusion that oral contraceptives protect against all PID to be premature, and urge caution in its application in health policy and clinical decisions.

Primary Tubal Infertility in Relation to the Use of an Intrauterine Device

J.R. Daling, N.S. Weiss, B.J. Metch, W.H. Chow, R.M. Soderstrom, D.E. Moore, L.R. Spadoni and B.V. Stadel. N Engl J Med 1985 Apr 11;312(15):937-41.

Women who use an intrauterine device (IUD) are at increased risk of acute pelvic inflammatory disease, but the relation of the IUD to subsequent infertility is not established. We interviewed 159 nulligravid women with tubal infertility to determine their prior use of an IUD. Their responses were compared with those of a matched group who conceived their first child at the time the infertile women started trying to become pregnant. The risk of primary tubal infertility in women who had ever used an IUD was 2.6 times that in women who had never used one (95% confidence interval, 1.3 to 5.2). The observed difference between cases and controls was not uniform for different types of IUD. The relative risk associated with use of a Dalkon Shield was 6.8 (1.8 to 25.2), and that associated with use of either a Lippes Loop or Saf-T Coil IUD was 3.2 (0.9 to 12.0). The smallest elevation in risk was found among users of copper-containing IUDs (relative risk, 1.9 (0.9 to 4.0) for all women who had ever used a copper-containing IUD). The relative risk for women who used only a copper-containing IUD was 1.3 (0.6 to 3.0). We conclude that use of the Dalkon Shield (and possibly of plastic IUDs other than those that contain copper) can lead to infertility in nulligravid women.

Tubal Infertility and the Intrauterine Device

D.W. Cramer, I. Schiff, S.C. Schoenbaum, M. Gibson, S. Belisle, B. Albrecht, R.J. Stillman, M.J. Berger, E. Wilson, B.V. Stadel, et al. N Engl J Med 1985 Apr 11;312(15):941-7.

To study the association between intrauterine devices (IUDs) and pelvic inflammatory disease, we compared contraceptive histories in 4,185 white women — 283 nulliparous women with primary tubal infertility, 69 women with secondary tubal infertility, and 3,833 women admitted for delivery at seven collaborating hospitals from 1981 to 1983. The relative risk of tubal infertility associated with IUD use was calculated by means of multivariate logistic regression to control for confounding factors, including region, year of menarche, religion, education, smoking, and reported number of sexual partners. The adjusted risk of primary tubal infertility associated with any IUD use before a first live birth was 2.0 (95% confidence limits, 1.5 to 2.6) relative to nonuse. Users of the Dalkon Shield had an adjusted risk of 3.3 (1.7 to 6.1), users of the Lippes Loop or Saf-T-Coil had a risk of 2.9 (1.7 to 5.2), and users of copper IUDs had a risk of 1.6 (1.1 to 2.4). Women who reported having only one sexual partner had no increased risk of primary tubal infertility associated with IUD use. The adjusted risk of secondary tubal infertility associated with use of a copper IUD after a first live birth was not statistically significant (1.5; 95% confidence limits, 0.8 to 3.0), whereas the risk from similar use of noncopper devices was significant (2.8; 1.3 to 5.9). We conclude that tubal infertility is associated with IUD use, but less so with copper IUDs.

Appendicitis Versus Pelvic Inflammatory Disease. A Diagnostic Dilemma

A.Z. Najem, D.J. Barillo, C.R. Spillert, J.C. Kerr and E.J. Lazaro. Am Surg 1985 Apr;51(4):217-22.

In order to determine whether any clinical or laboratory findings were helpful in differentiating acute appendicitis (AP) from acute pelvic inflammatory disease (PID), this retrospective study was undertaken. Records of all female patients 12 to 50 years of age, undergoing laparotomy with a preoperative diagnosis of AP over the past 15 years, were reviewed and pertinent data recorded. In comparing AP (n = 106) with PID (n = 39), longer duration of symptoms, relationship of onset of pain to the menstrual cycle, and frequent requests for gynecological consultation distinguished the PID from the AP cases. Although complete reliance cannot be placed on any clinical or laboratory finding in differentiating AP from PID, the final satisfactory outcome justifies laparotomy when the diagnosis cannot be established by other means.

Role of Sexual Behavior in the Development of Pelvic Inflammatory Disease

W. Newton and L.G. Keith. J Reprod Med 1985 Feb;30(2):82-8.

The role of sexual behavior in the development of pelvic inflammatory disease (PID) is not well understood. In general, the literature is limited and flawed in the methods used to assess sexual behavior. Good evidence suggests that PID in Western society is a sexually transmitted disease. For number of partners, frequency of intercourse, time of intercourse, and sexual life-style the evidence suggests that those variables have a significant role in the development of PID. It is important to assess PID in the context of all its risk factors, including sexual behavior, race, prior history of PID, and IUD use.

Influence of Removal of Intrauterine Contraceptive Devices on Colonization of the Cervix by Actinomyces-Like Organisms

K. Mao and J. Guillebaud. Contraception 1984 Dec;30(6):535-44.

An overall prevalence rate of actinomyces-like organisms (ALO) in cervical smears from intrauterine contraceptive device (IUCD) users of 3 percent (79/2, 734) was found, with a rate of 2 percent and 22.6 percent for copper and inert IUCD users. Although the users of the inert IUCDs were older, and their devices had been in situ longer, these factors did not account for the significant difference between the two types of IUCD. Fifty-five patients were counselled and given a leaflet on ALO. Fourteen IUCD users with ALO positive smears who had their devices removed had mild or moderate pelvic pain or discharge. Six others who were asymptomatic had the IUCD removed at their own request. All fifty-five patients were re-examined six months to one year later, and a smear was repeated. Only one woman required later removal of the IUCD because of dyspareunia with pelvic tenderness. After removal of the IUCD, and without antibiotic therapy, in 100 percent (20/20) of the women, ALO colonization was no longer found six to twelve months later. This applied even to seven women who had had a new copper IUCD inserted immediately after removal of the index device.

Laboratory Diagnosis

Comparison of Endometrial Biopsy and Peritoneal Fluid Cytologic Testing with Laparoscopy in the Diagnosis of Acute Pelvic Inflammatory Disease

J. Paavonen, R. Aine, K. Teisala, P.K. Heinonen and R. Punnonen. Am J Obstet Gynecol 1985 Mar 1;151(5):645-50.

Twenty-seven women with suspected acute pelvic inflammatory disease were studied by laparoscopy and endometrial biopsy. Overall, 67 percent (18 of 27) of the women had acute salpingitis at laparoscopy, 70 percent (19 of 27) had plasma cell endometritis, and 67 percent (10 of 15) had an inflammatory cytologic pattern of the peritoneal fluid. In comparison to laparoscopically detected salpingitis, endometritis detected with biopsy had a sensitivity of 89 percent, a specificity of 67 percent, a positive predictive value of 84 percent, and a false negative rate of 22 percent in the diagnosis of pelvic inflammatory disease. The corresponding figures for inflammation of the peritoneal fluid were 75 percent, 67 percent, 90 percent, and 25 percent. This study demonstrates that nonpuerperal endometritis is an entity associated with pelvic inflammatory disease, most likely representing an intermediate stage between cervicitis and salpingitis. Endometrial biopsy as an office procedure is a good alternative to laparoscopy in the diagnosis of acute pelvic inflammatory disease and may in fact detect early cases not yet visible at laparoscopy.

Therapy

The Polymicrobial Etiology of Acute Pelvic Inflammatory Disease and Treatment Regimens

M.G. Dodson and S. Faro. Rev Infect Dis 1985 Nov-Dec;7 Suppl 4:S696-702.

Continued research on acute pelvic inflammatory disease (PID) has demonstrated that PID has a rather remarkably varied etiology, the pathogens responsible including *Neisseria gonorrhoeae*, *Chlamydia trachomatis*, aerobic and anaerobic gram-positive and gram-negative organisms, and possibly mycoplasmas. There is clearly no single antimicrobial agent that is effective against all of the organisms implicated in the etiology of acute PID. The aminoglycosides, generally in combination with an antibiotic such as clindamycin, are commonly used in the treatment of patients with acute PID. The combination of a new monocyclic beta-lactam antibiotic, aztreonam, and clindamycin may be less toxic and equally or more effective for the treatment of acute PID.

The Next 10 Years in the Treatment of Pelvic Infections

W.J. Ledger. Am J Med 1985 Jun 28;78(6B):194-203.

The future developments in the treatment of pelvic infections in women are based on recent changes. There is an expanded knowledge of the complex multibacterial nature of pelvic infections, the clinical view of salpingitis has radically changed, and there have been great modifications in antibiotic treatment strategies with particular emphasis on anaerobes and chlamydia. In the next 10 years, the following new developments may be expected. In the diagnosis of pelvic infection, there will be new efforts to have better clinical tests and the use of nonspecific and specific laboratory tests. The rapid identification of *Neisseria gonorrhoeae*, group B beta-hemolytic streptococcus, chlamydia, and *Bacteroides fragilis* would be an important laboratory aid. The treatment of pelvic infection will not be significantly altered by the introduction of new antibiotics. There will be an emphasis on new combinations of currently available antibiotics and studies that focus on the long-term follow-up of treated patients. In the understanding of the pathophysiology of pelvic infections, the importance of the spermatozoa as a carrier of bacteria and the potent immunosuppression due to seminal fluid will be investigated in detail, along with a greater emphasis on treatment of the male.

Choice of Antibiotics and Length of Therapy in the Treatment of Acute Salpingitis

G.R. Monif. Am J Med 1985 Jun 28;78(6B):188-93.

This article reviews the rationale for the therapy of acute salpingitis and the conceptual basis for the length of therapy. The key to therapy of acute salpingitis is the need to accommodate polymicrobial etiology, polymicrobial bacterial superinfection, and the potential presence of penicillinase-producing strains of *Neisseria gonorrhoeae* into a therapeutic equation that has been determined by the appropriate staging of disease. The anticipated therapeutic response identified for monomicrobial disease due to *Neisseria gonorrhoeae* constitutes the end titration point for drug administration. Duration of continued therapy beyond this point is governed by the need to complete therapy for *Chlamydia trachomatis* or to assure resolution of advanced disease.

Risk Factors for Postcesarean Endomyometritis

M.L. Yonekura. Am J Med 1985 Jun 28;78(6B):177-87.

Postcesarean endomyometritis is the most common nosocomial infection treated by obstetrician/gynecologists. One important prevention strategy is the use of perioperative antibiotic prophylaxis initiated after occlusion of the umbilical cord for parturient patients with a high risk of this infection. However, the identification of these high risk patients remains problematic. Numerous clinical risk factors have been identified in the literature. Important intrinsic risk factors include indigent socioeconomic status, anemia, and preterm gestational age at the time of cesarean section. The three most consistently identified extrinsic risk factors include labor prior to cesarean section, the duration of ruptured chorioamniotic membranes, and the number of preoperative vaginal examinations. Alternatively, many investigators have attempted to define high-risk patients utilizing various laboratory tests, such as Gram staining or bacterial culture of amniotic fluid, chorioamniotic membranes, or endometrial biopsy specimens; although specific, these tests have not been sufficiently sensitive predictors of infection. Currently, assessment of the duration of ruptured membranes and length of labor remain the most sensitive, readily available, and therefore clinically useful predictors of postcesarean endomyometritis.

Introductory Address: Treatment of Pelvic Inflammatory Disease in View of Etiology and Risk Factors

L. Westrom. Sex Transm Dis 1984 Oct-Dec;11(4 Suppl):437-40

Pelvic inflammatory disease is a common infection that, from an etiologic point of view, is strongly correlated with the presence of sexually transmissible microorganisms. A part from exposure to such agents, risk factors include youth, minor gynecologic surgery, earlier episodes of salpingitis, and the use of intrauterine contraceptive devices. For the prevention of pelvic inflammatory disease, consideration of these risk factors is important. The vast majority of fallopian tube infections are caused by the ascending spread of sexually transmissible agents or endogenous vaginal organisms through the genital tract. The multitude of etiologic agents must be considered in the choice of therapy, and double or triple treatment regimens may be appropriate.

Aztreonam Plus Clindamycin as Therapy for Pelvic Infections in Women

J.G. Pastorek, II, C. Cole, K.E. Aldridge and J.C. Crapanzano. Am J Med 1985 Feb 8;78(2A):47-50

Aztreonam, a new monobactam antibiotic with specific gram-negative aerobic activity, was used in combination with clindamycin in the treatment of 40 women with pelvic infection, including post-partum endometritis, pelvic inflammatory disease, and post-hysterectomy pelvic cellulitis. Clinical cure was achieved in 87 percent of patients. Failure was related to the limited gram-positive aerobic spectrum of clindamycin. All aerobic gram-negative enteric organisms were sensitive in vitro to less than 0.125 microgram/ml of aztreonam.

Cefotaxime Treatment for Women with Community-Acquired Pelvic Abscesses

D.L. Hemsell, R. Santos-Ramos, F.G. Cunningham, B.J. Nobles and P.G. Hemsell. Am J Obstet Gynecol 1985 Mar 15;151(6):771-7.

Forty-one women with pelvic abscesses complicating salpingitis were treated with parenteral cefotaxime, a newer cephalosporin. Abscesses ranged in size from 4 by 4 to 13 by 15 cm, and in 10 women (24%) they were greater than or equal to 10 cm. *Neisseria gonorrhoeae* was recovered from the endocervix in 17 women (41%). A mean of 26.7 gm of cefotaxime was given over a mean of 6.5 days, and operation was not required during initial therapy. Only two women (5%) required the addition of another antimicrobial. Chronic pelvic pain and recurrent infection were infrequent during the 31- to 43-month follow-up period. Five women (12%) were readmitted for elective surgical therapy because of persistent or recurrent adnexal mass 1 to 33 months following study entry. Six (15%) women became pregnant and were delivered of their infants a mean of 25 months following cefotaxime therapy.

Research and Evaluation

Prevalence of Antibodies to *Chlamydia trachomatis, Neisseria gonorrhoeae,* and *Mycoplasma hominis* in Infertile Women

K.H. Tjiam, G.H. Zeilmaker, A.T. Alberda, B.Y. van Heijst, J.C. de Roo, A.A. Polak Vogelzang, T. van Joost, E. Stolz and M.F. Michel. Genitourin Med 1985 Jun;61(3):175-8.

A total of 57 infertile women, who had been referred for in vitro fertilization or for diagnostic laparoscopy, were tested for the presence of antibodies to *Chlamydia trachomatis*, *Neisseria gonorrhoeae*, and *Mycoplasma hominis*. Four were excluded from the study. Of the remaining 53, 33 had laparoscopically obvious tubal disorders, such as adhesions, distal occlusions and strictures, and 20 did not. Antibodies to *C. trachomatis* were found in 7/33 (21.2%) v 0/20, antibodies to *N. gonorrhoeae* in 20/38 (60.6%) v 5/20 (25%), and antibodies to *M. hominis* in 18/24 (75%) women with tubal disorders v 13/19 (68.4%) of those with no disorder. Antibodies to *C. trachomatis* and *N. gonorrhoeae* were significantly (p less than 0.05) more common in women with tubal disorders. The high prevalence of antibodies to *N. gonorrhoeae* in infertile women without tubal disorders suggests that ciliated tubal epithelium is damaged after inflammation without this being laparoscopically visible. Our results confirm the important role of *N. gonorrhoeae* and *C. trachomatis* in the etiology of infertility after tubal inflammation.

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*Abstracted

Genital Mycoplasma Infection

Clinical

Serological Evidence that Chlamydiae and Mycoplasmas are Involved in Infertility of Women

B.R. Mller, D. Taylor-Robinson, P.M. Furr, B. Toft and J. Allen. J Reprod Fertil 1985 Jan;73(1):237-40

Women with a history of infertility for 2 or more years were examined by hysterosalpingography (HSG) and antibodies against *Chlamydia trachomatis*, *Mycoplasma hominis* and *M. genitalium* were measured by a microimmunofluorescence technique in sera obtained immediately before HSG. Of 45 women with abnormal HSG findings, 15 (33%) had antibodies to *C. trachomatis* and 16 (35.5%) to *M. hominis*. In contrast, of 61 women with normal HSG findings, only 8 (13%) and 7 (11.5%) had antibodies to these microorganisms, respectively. Antibody against *M. genitalium* was found in 26 of the patients (20% abnormal HSG and 28% normal HSG), indicating the need for further investigation of the significance of this mycoplasma in female infertility. The present results do confirm, however, that *C. trachomatis* is an important cause of infertility in women and suggest strongly that *M. hominis* is implicated.

Importance of *Mycoplasma hominis* in Acute Salpingitis Assessed by Culture and Serological Tests

K. Lind, G.B. Kristensen, A.C. Bollerup, P. Ladehoff, S. Larsen, A. Marushak, P. Rasmussen, J. Rolschau and I. Skoven, T. Srensen, et al. Genitourin Med 1985 Jun;61(3):185-9.

In 95 women with a provisional diagnosis of pelvic inflammatory disease, a final diagnosis of acute salpingitis was confirmed by laparoscopy in 46 and 10 had strong clinical evidence of acute salpingitis. The findings in the remaining 39 patients without signs of acute salpingitis by laparoscopy were used as a standard of reference. Criteria for the diagnosis of possible mycoplasmal salpingitis were tentatively defined as the isolation of *Mycoplasma hominis* from the cervix together with positive test results for *M. hominis* antibodies (a titre of greater than or equal to 1/1280 or a change in titre, or both); these criteria were fulfilled in 12 patients with acute salpingitis. A positive correlation between mycoplasmal salpingitis and chlamydial salpingitis or gonococcal salpingitis, or both, was significant. Mycoplasmal salpingitis was not associated with any characteristic clinical feature different from those of patients with non-mycoplasmal salpingitis. Our findings do not support the view that *M. hominis* is an important primary pathogen in acute salpingitis.

Neonatal Mycoplasmaemia: *Mycoplasma hominis* as a Significant Cause of Disease?

P.F. Unsworth, D. Taylor-Robinson, E.E. Shoo and P.M. Furr. J Infect 1985 Mar;10(2):163-8.

A full-term baby boy had respiratory distress, fever, and pneumonia within 20 hours of birth. Isolation of *Mycoplasma hominis* from blood taken after 20 hours and 11 days was accompanied by an antibody response. Although chlamydial IgM antibody was detected, chlamydial infection probably did not cause the pneumonia. Penicillin was ineffective, but treatment with gentamicin, and particularly tetracycline, was associated with slow improvement. *Mycoplasma hominis* should be considered as a cause of respiratory disease and fever in neonates.

Ureaplasma-Infected Human Sperm in Infertile Men

K. Grossgebauer and A. Hennig. Arch Androl 1984;12 Suppl:35-41.

The case of an infertile man with oligospermia and symptoms of urethritis-prostatitis, whose spouse had a vaginal discharge, is reported. Microbiological analysis of appropriate specimens revealed a strain of tetracycline-resistant *Ureaplasma urealyticum* in both patients. Using the transmission electron microscope, it was possible to demonstrate spermatozoal heads "infected" with microorganisms strongly resembling *Ureaplasma urealyticum*.

The Role of Mycoplasmas in Sexually Transmitted Vaginitis

G.F. Altomare, M.M. Polenghi, P.D. Pigatto, G. Bella, R. Vivanti and P. Italiano. Boll Ist Sieroter Milan 1984 Sep;63(4):348-51

Mycoplasmas were isolated from 325 female subjects who came to a gynecological outpatient clinic for many different reasons. Microorganisms can also be isolated in a high percentage from apparently healthy subjects. Our data indicate that mycoplasma can be either simple commensals in the urogenital apparatus or saprophytes. In vulvovaginitis, mycoplasma can cause a type of pathology which is always associated with the presence of other pathogens.

Therapy

In Vitro Activity of Ciprofloxacin against *Chlamydia trachomatis* and *Ureaplasma urealyticum*

F. Rumpianesi, V. Sambri, S. Bertini, I. Tamba and R. Cevenini. Chemioterapia 1984 Jun;3(3):173-4.

The in vitro activity of ciprofloxacin against 5 strains of *Chlamydia trachomatis* and 5 strains of *Ureaplasma urealyticum* was tested. Both *C. trachomatis* and *U. urealyticum* showed a certain degree of variability in their susceptibility to the drug. The minimum inhibitory concentration (MIC) of ciprofloxacin against *C. trachomatis* was 1 micrograms/ml, whereas the minimum bactericidal concentration was greater than or equal to 10 micrograms/ml. The MIC of ciprofloxacin against *U. urealyticum* was 1 micrograms/ml for 3 strains and higher than 10 micrograms/ml for two strains.

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*Abstracted

Sexually Transmitted Diseases—General

Clinical

Urinary Tract Infection in Sexually Active Homosexual Men

R.C. Barnes, R. Daifuku, R.E. Roddy and W.E. Stamm. Lancet 1986 Jan 25;1(8474):171-3.

Fourteen of 280 young, sexually active men with acute urinary symptoms had pronounced bacteriuria—13 with *Escherichia coli* and 1 with *Staphylococcus saprophyticus.* Twelve of the 14 bacteriuric men were homosexual or bisexual, compared with three of 22 non-bacteriuric control patients. Pyuria and symptoms of cystitis were more common in the bacteriuric men, and these men frequently had a urethral discharge on examination, and nongonococcal urethritis on gram stain of the discharge. The *E. coli* strains causing cystourethritis in these men showed properties previously associated with acute urinary tract infection in women, including O serotype, hemolysin production, mannose-resistant hemagglutination of human erythrocytes, and P-fimbriation. Sexually active homosexual men are a newly identified group at increased risk of acute urinary tract infection, and *E. coli* may contribute to nongonococcal urethritis in this population.

Pattern of Sexually Transmitted Disease in Madurai, India

P. Jeyasingh, T.B. Ramanaiah and S.D. Fernandes. Genitourin Med 1985 Dec;61(6):399-403.

The pattern of sexually transmitted disease (STD) in a public clinic in Madurai City, India, was studied for 10 years (1974-83). Syphilis was found to be the most common STD in men (28.3%) and trichomoniasis in women (39.6%). The tropical STDs (chancroid, lymphogranuloma venereum, and granuloma inguinale) formed a sizeable proportion (30.1%) of all STDs. A tendency to overdiagnose chancroid and lymphogranuloma venereum and a failure to detect many cases of gonorrhea reflected a lack of laboratory facilities.

The Validity of the Leukocyte Esterase Reagent Test Strip in Detecting Significant Leukocyturia

G.P. Marquette, T. Dillard, S. Bietla and J.R. Niebyl. Am J Obstet Gynecol 1985 Dec 15;153(8):888-9.

This prospective trial demonstrated that the best possible definition for a positive leukocyte esterase test (Chemstrip 9) is + or ++. With use of this definition, the sensitivity in detecting significant leukocyturia is 83 percent and the specificity is 70 percent. The use of this test strip could reduce screening costs in registering obstetric patients.

Microbiology of the Lower Genital Tract in Postmenarchal Adolescent Girls: Differences by Sexual Activity, Contraception, and Presence of Nonspecific Vaginitis

M.A. Shafer, R.L. Sweet, M.J. Ohm-Smith, J. Shalwitz, A. Beck and J. Schachter. J Pediatr 1985 Dec;107(6):974-81.

The prevalence of selected microorganisms in the lower genital tract in postmenarchal adolescent girls was assessed, including vaginal *Gardnerella vaginalis*, group B streptococcus, lactobacillus, mycoplasma species, *Ureaplasma urealyticum*, *Staphylococcus aureus*, and yeast, and endocervical mycoplasma species, *U. urealyticum*, *Chlamydia trachomatis*, *Neisseria gonorrhoeae*, and *Trichomonas vaginalis*. Specific attention was focused on important sexually transmitted disease organisms, and differences in isolations by age, sexual activity, ethnicity, contraception, and the diagnosis of nonspecific vaginitis were measured. Sexually active subjects had a mean of 6.05 organisms (SD = 3.16), compared with 3.12 organisms (SD = 3.92) in non-sexually active subjects ($P = 0.001$). Sexually active subjects had significantly more vaginal *G. vaginalis*, lactobacilli, mycoplasma species, and *U. urealyticum*, as well as endocervical mycoplasma species and *U. urealyticum*, compared with non-sexually active subjects; *C. trachomatis*, *N. gonorrhoeae*, and *T. vaginalis* were isolated exclusively from the sexually active group. Significant differences in isolation rates by ethnicity were found in vaginal mycoplasma species and *U. urealyticum*, and endocervical mycoplasma species, *U. urealyticum*, *C. trachomatis*, *N. gonorrhoeae*, and *T. vaginalis*. In general, organisms were isolated from blacks most frequently; *N. gonorrhoeae* was isolated from blacks exclusively. Differences were found in microbiologic isolations by the presence or absence of nonspecific vaginitis. Vaginal *G. vaginalis* and mycoplasma species and endocervical mycoplasma species and *U. urealyticum* were found significantly more often in isolates from the group with nonspecific vaginitis. It is important to define the microbial flora of the lower genital tract in adolescent girls in order to understand its role in the pathogenesis of acute salpingitis.

Leukocyte Esterase Activity in the Rapid Detection of Urinary Tract and Lower Genital Tract Infections in Obstetric Patients

I.A. Abbasi, L.W. Hess, T.R. Johnson, E. McFadden and B. Chernow. Am J Perinatol 1985 Oct;2(4):311-3.

Infections of the vagina and urinary tract are important problems for the obstetrician. Examination of the vaginal discharge and urine for the presence of leukocytes is an important part of the evaluation for vaginitis and urinary tract infections. Neutrophils contain several esterases that are not present in serum, urine, or vaginal secretions. These esterases are not influenced by bacteria, commonly used drugs, or variable compositions of urine or vaginal secretions. A prospective study was performed to assess the sensitivity and specificity of leukocyte esterase activity as measured by dipstick (Chemstrip 9, Biodynamics) for the prediction of vaginitis and urinary tract infections during pregnancy. Results were compared with those obtained from potassium hydroxide smears, wet preps, and urine cultures. The vaginal discharge and urine of 65 patients was tested for leukocyte esterase activity on their initial OB visit. Leukocyte esterase was 100 percent sensitive and 100 percent specific for detecting urinary tract infections. It was 100 percent sensitive and 90 percent specific for predicting vaginal infections. Trichomonas infections accounted for the positive leukocyte esterase results when the urine culture was negative. On the basis of this study, we believe that leukocyte esterase activity is sufficiently sensitive and specific to permit use of this test as a rapid and inexpensive screening procedure for vaginitis and urinary tract infections.

Counseling the Sexually Active Teenager: Reflections from Pediatric Practice

K.R. Sladkin. Pediatrics 1985 Oct;76(4 Pt 2):681-4.

Counseling the sexually active teenager is both an important and a difficult undertaking. Due to the increasing rates in adolescent sexual intercourse, pregnancy, and sexually transmitted diseases, it is necessary for all health care professionals to elicit a sexual history from each patient. Being comfortable with one's own sexuality and conveying complete confidentiality are the sine qua non of this type of interview and counseling. Topics that may be covered are contraception, sexually transmitted diseases, sexual intercourse and its place in the adolescent's life, other kinds of sexual expression, and satisfaction with one's sexuality. It is not necessary to have liberal views of sexuality to obtain an adequate history or to provide competent counseling.

Pilot Study of Cervical Cytology Screening in a Sexually Transmitted Diseases Clinic

H. Lyttle, W.M. Platts and A.B. MacLean. Genitourin Med 1985 Oct;61(5):330-4.

A pilot study of cervical cytology was carried out on 500 new patients at the women's sexually transmitted disease (STD) clinic at this hospital. The aim was to discover the incidence of abnormal smears in order to gauge the worth of cervical cytology as a routine clinic procedure. Information was also gathered on each patient's age, sexual history, method of contraception used, previous smears, and genital infection. Smears showing carcinoma in situ, dysplasia, or warty atypia were regarded as abnormal, and the relevant patients were referred for colposcopy. Seventy-three (14.6%) had abnormal smears. Eight women (1.6%), average age 29.7 years, had cervical intraepithelial neoplasia grade III (CIN III) confirmed by histology. One-third of the patients with abnormal smears had genital warts, and the incidence of abnormal smears was greater in patients with genital warts than in those without warts. We concluded that STD clinics are useful places in which to carry out cervical cytology screening, and we noted a positive association between infection with genital warts and abnormal smears.

Comparative Rates of Sexually Transmitted Diseases Among Heterosexual Men, Homosexual Men, and Heterosexual Women

S.L. Short, D.L. Stockman, S.M. Wolinsky, M.A. Trupei, J. Moore and R.C. Reichman. Sex Transm Dis 1984 Oct-Dec;11(4):271-4

The prevalences of several sexually transmitted diseases (STD) among patients attending a public STD clinic were determined in a prospective study. Rates of gonorrhea, syphilis, genital herpes, trichomoniasis, nongonococcal urethritis, pediculosis pubis, scabies, and venereal warts were ascertained according to sex, sexual preference, and race. Numbers of cases of diseases not routinely reported to most public health agencies exceeded numbers of cases of diseases that are routinely reported. Rates of gonorrhea were higher among men than among women and higher among blacks than among whites. Syphilis was most common among homosexual men. Trichomoniasis was three times more frequent among blacks than among whites. Rates of nongonococcal urethritis among heterosexual men were almost twice those among homosexual men. Whites were more likely than blacks to have pediculosis pubis, scabies, and venereal warts. STD not routinely reported to most public health agencies are commonly seen in public clinics, and rates vary according to sex, sexual preference, and race.

Are We Failing Our Teenagers? Value of a Family Planning Service for Teenagers Within the Sexually Transmitted Disease Clinic

J.M. Tobin and R.B. Roy. Br Med J (Clin Res) 1985 Feb 2;290(6465):376-8

Out of 100 teenage girls attending a sexually transmitted disease clinic for the first time, 77 were found to be using a reliable method of contraception and had similar characteristics to teenage girls attending a family planning clinic. The 23 girls not using any reliable contraception exhibited a different pattern of sexual behavior and were at high risk of unplanned pregnancy. Subsequently, another group of 23 girls not using contraception when seen at the sexually transmitted disease clinic were actively encouraged to attend a family planning clinic. Their risk of unplanned pregnancy was much reduced, although their pattern of sexual activity was unchanged. Ready availability of contraceptive advice for unprotected teenagers in sexually transmitted disease clinics would reduce their high risk of unplanned pregnancy.

Sexually Transmitted Diseases: An Epidemic in Adolescent Girls?

G.E. Forster, G.E. Robinson and P.E. Munday. Br J Vener Dis 1984 Dec;60(6):402-5

The prevalence of sexually transmitted disease (STD) in adolescent girls aged 15-19 attending a department of genitourinary medicine was compared for the years 1972 and 1982. Data were obtained from the confidential register using the coding of the clinic returns to the Department of Health (form SBH 60). There were 1,373 patients in 1972 and 1,799 in 1982, 6.4 percent and 7 percent, respectively, of the total female clinic population. The prevalence of syphilis, gonorrhea, and infection with *Trichomonas vaginalis*, herpes simplex virus, and warts was almost unchanged. Other conditions, which are not classified as STD, were largely responsible for the increase in new attendances, the prevalence of these conditions having nearly doubled over the ten year period. Thus an epidemic of STD has not been shown in this adolescent female population over the past decade.

Postponing Sexual Involvement Among Adolescents. An Alternative Approach to Prevention of Sexually Transmitted Diseases

M. Howard. J Adolesc Health Care 1985 Jul;6(4):271-7.

Over 1,000 teenagers participated in the field test of an educational series designed to help them resist the social and peer pressures that can lead to early sexual involvement. A companion program for parents was designed to help adults better understand the pressures experienced by adolescents and aid the parents in reinforcing the information, given to their children. Initial findings indicate skill building may be an important addition to the knowledge-based curriculum commonly used to prevent the spread of sexually transmitted disease among teenagers today.

Adolescence and Sexual Behavior. Trends and Implications for STD

K.R. O'Reilly and S.O. Aral. J Adolesc Health Care 1985 Jul;6(4):262-70.

Teenage sexual activity became more common in the 1970s, and that trend may continue in this decade. Teenagers have thus established themselves as an important component of the population at risk of sexually transmitted disease (STD). Adolescents exhibit many of the same features of sexual behavior seen in the adult population. However, adolescents' abilities to recognize, evaluate symptoms of, and seek treatment for STD are generally limited. Many teenagers are hesitant to admit that they have begun sexual activity or that something like STD could happen to them. The combination of these factors, with generally liberalizing trends in sexual behavior in the last decade, has elevated the risk of STD for teenagers and made the job of adolescent health care providers more difficult.

The Association of Sexually Transmitted Diseases with Cervical Intraepithelial Neoplasia: A Case-Control Study

F.B. Guijon, M. Paraskevas and R. Brunham. Am J Obstet Gynecol 1985 Jan 15;151(2):185-90

Thirty-three women with histologically confirmed cervical intraepithelial neoplasia (grades I to III, with one case of microinvasive carcinoma) and 54 women without evidence of the disease were prospectively studied to determine the relationship of genital infection to cervical neoplasia. Demographic and sexual data for patients and control subjects were collected, with standardized clinical and colposcopic evaluation by means of predefined diagnostic categories. Cultures from the cervix were examined for herpes simplex virus, cytomegalovirus, *Chlamydia trachomatis*, and *Neisseria gonorrhoeae*. Human papillomavirus infection was identified by characteristic changes of koilocytosis in cytologic or histopathologic specimen. Cultures from the vagina were evaluated for *Gardnerella vaginalis*, *Trichomonas vaginalis*, *Ureaplasma urealyticum*, *Mycoplasma hominis*, *Candida albicans*, and other yeasts. Separate Gram strains were prepared from endocervical secretions and from vaginal secretions. More lifetime sexual partners, larger area of transformation zone, evidence of human papillomavirus infection, and altered vaginal flora were observed in women with cervical intraepithelial neoplasia. The association of human papillomavirus infection and altered vaginal flora with cervical intraepithelial neoplasia was independent of sexual experience.

Inflammatory Conditions and Semen Quality among Subfertile Sudanese Males

E.F. Omer. Trop Doct 1985 Jan;15(1):27-8.

Fifty-nine subfertile males were investigated to assess seminal quality, inflammatory conditions and spermatogenic picture in relation to their subfertility. Defects in semen analysis were found associated with an old gonococcal infection (42.4%), schistosomiasis (13.6%) and chronic prostatitis (5.1%). Varicocele was observed in a few patients (3.4%). Azoospermia was found in 40.7 percent, of whom 33.3 percent were found to suffer from spermatogenic arrest.

Physician Attitudes Toward Confidential Care for Adolescents

J. Lovett and M.S. Wald. J Pediatr 1985 Mar;106(3):517-21.

We examined factors that determine whether pediatricians will grant confidential care to adolescents. Through four vignettes, in which adolescents of different ages and maturity requested confidential care, we assessed the willingness of physicians to give such care for four problems: request for contraceptive, diagnosis of gonorrhea, intrauterine device found incidentally on x-ray study, and illicit drug use. A random sample of 932 physicians responded to the vignettes. Overall, physicians agreed to give confidential care to adolescents in 75 percent of the vignettes. They were more likely to give confidentiality in cases involving sexual activity. They supported confidential care for 87 percent of patients requesting contraceptives, but for only 54 percent reporting illicit drug use. The proportion of physicians supporting confidentiality increased with age and maturity of the minors. Seventeen-year-old mature adolescents seeking contraceptives were given confidentiality by 97 percent of physicians. Thus physician responses to vignettes indicated that they strongly support confidential care for adolescents as represented in the clinical vignettes.

Cell-Mediated and Humoral Immune Responses to Chlamydial and Herpesvirus Antigens in Patients with Cervical Carcinoma

E. Qvigstad, M. Onsrud, M. Degre and K. Skaug. Gynecol Oncol 1985 Feb;20(2):184-9.

Herpes simplex virus (HSV) and *Chlamydia trachomatis* are both discussed in the etiology of cervical carcinoma. In this study, the antibody titers and the T-cell proliferative responses to chlamydial and HSV antigens in patients with cervical intraepithelial neoplasia (CIN) and invasive cervical cancer have been investigated and compared. The patients with CIN and invasive cancer showed approximately the same degree of immune responses to chlamydial and HSV antigens. Of the patients, 58 percent showed proliferative T-cell responses to *C. trachomatis* antigen, 87 percent to HSV antigens. Chlamydial antibodies were detected in 65 percent of the patients, while 81 percent had a positive HSV serology. Our results show a lack of correlation between levels of antibody titer and T-cell responses. It is concluded that patients with CIN and invasive cervical cancer have intact cellular immune responses to both chlamydial and HSV antigens. The eventual role of these infections in the etiology remains unclear.

Sexually Abused Children: Identifying Masked Presentations in a Medical Setting

R.S. Hunter, N. Kilstrom and F. Loda. Child Abuse Negl 1985;9(1):17-25.

Sexual abuse of children frequently lies hidden while the victims receive medical care for other complaints. To identify clinical signals of latent abuse, we studied 50 children whose initial presentations masked the presence of sexual abuse and compared them with 31 overt cases identified by chief complaint. A broad variety of symptoms masked the abuse. While some, such as early adolescent pregnancy and genital symptomatology, might have suggested the diagnosis, unusual physical symptoms, psychosomatic, and behavioral disorders were as frequent. The masked group differed significantly from the more frequently studied overt group in that chronic history of sexual abuse was twice as common; school problems and psychosomatic disorders were three times as frequent; the alleged abuser was more often an immediate family member, usually the father; male victims were more likely to present in this disguised manner. Familiarity with typical masked presentations should aid earlier identification of these troubled children.

Recognition of Hypochondriasis in a Clinic for Sexually Transmitted Disease

D.P. Frost. Genitourin Med 1985 Apr;61(2):133-7.

A descriptive study of 100 consecutive patients referred for psychiatric assessment from a clinic for sexually transmitted disease (STD) is reported. Thirty-six patients presented with physical symptoms for which no organic cause could be found. Various physical and psychological features of the overall presentation of this "somatic" group were identified. These are discussed in terms of diagnostic categories, etiological mechanisms, and theories of illness behavior. The importance of directly observable aspects of the patients' consultation behavior is stressed over and above deep psychological constructs. The diagnosis of hypochondriasis is seen as essentially a medical one, which entails the doctor making a set of judgements that require a broad clinical perspective.

Problems of Adolescent Sex

P. Senanayake. Int J Gynaecol Obstet 1984 Dec;22(6): 457-61.

Four issues concerning adolescent sexuality are reviewed—the counselling needs of teenagers, the risks of sexually transmitted diseases, the controversy over contraception for adolescents, and the consequences of pregnancy in adolescence—in terms of their effect on the adolescent as an individual, and on the community of which he/she belongs. The need for services specifically designed for adolescents is stressed, demonstrating that many of the "problems" of adolescent sex can be successfully addressed through comprehensively planned and executed programs.

Microorganisms in Semen Used for Artificial Insemination

J.L. Leiva, E.M. Peterson, M. Wetkowski, L.M. de la Maza and S.C. Stone. Obstet Gynecol 1985 May;65(5):669-72.

The effect of freezing semen in a cryopreservative media consisting of egg yolk glycerol with or without erythromycin was tested for its effect on the viability of microorganisms present in donor semen and on sexually transmitted pathogens seeded into semen. All donor semen contained two or three species of microorganisms that could be considered skin flora. Five of ten donor semen specimens contained *Ureaplasma urealyticum* that was not affected by either freezing or antimicrobial treatment. Some strains of *Neisseria gonorrhoeae*, when seeded into semen, survived all conditions except freezing in egg yolk glycerol containing erythromycin. *Chlamydia trachomatis* was erradicated when erythromycin was present in the cryopreservative. There was no detectable effect of any treatment tested on the survival of herpes simplex virus.

Chlamydia, Mycoplasmas, Ureaplasmas, and Yeasts in the Lower Genital Tract of Females. Comparison Between a Group Attending a Venereal Disease Clinic and a Control Group

B.R. Mller, A. Sparre Jrgensen, E. From and A. Stenderup. Acta Obstet Gynecol Scand 1985;64(2):145-9.

One hundred sixty-two women were investigated. Group I consisted of 85 women, who were partners to men with nongonococcal urethritis (NGU) or presented macroscopic signs of cervicitis; patients who had harbored *Neisseria gonorrhoeae* were excluded from the study. Group II was a control group of 77 women without any complaints from the urogenital tract and with normal findings at pelvic examination. All the women were tested for infection with *Chlamydia trachomatis, Mycoplasma hominis, Ureaplasma urealyticum*, and *Candida albicans*. In group I, chlamydiae and mycoplasmas were recovered in 44 percent and 36 percent, respectively, the corresponding figures for the control group (group II) being 5 percent and 19 percent. The difference is highly significant. No such difference between the two groups was found for ureaplasmas. Sixteen percent of the patients in group I were positive for *C. albicans*; 12 percent were positive in group II. Fifty percent of asymptomatic NGU-partners were chlamydia-positive, and about one-third of patients with either dysuria or vaginal discharge harbored the organism. No difference in the isolation frequency of mycoplasmas was observed between asymptomatic partners to male NGU carriers and women with increased vaginal discharge, whereas the organism was isolated more frequently from patients with dysuria. Fifty-nine percent of patients with cervicitis were chlamydia-positive, compared with 30 percent of patients with normal cervical appearance and normal vaginal discharge. Samples obtained from the cervix were more often positive than samples from the urethra. In conclusion, if samples can be taken from only one of the two sites in patients with lower genital tract infection, the cervix is the optimal sampling site.

Research and Evaluation

Tracing Contacts of Persons with Sexually Transmitted Diseases in a Developing Country

J. Winfield and A.S. Latif. Sex Transm Dis 1985 Jan-Mar;12(1):5-7.

A simplified system for tracing of contacts of patients suffering from sexually transmitted diseases is presented. Use of a contact card given to the index case led 341 contacts (19.8%) to attend a clinic for treatment voluntarily. Visits to the homes of contacts who did not bring their cards to the clinics were made by health assistants employed by the local health department. After being traced in this manner, a further 367 contacts (21.3%) were seen. No substantial cost was born by the department, and the exercise did not necessitate the employment of additional staff.

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Sexually Transmitted Diseases—Other

Candidiasis

The Influence of Antibiotics on the Growth of *Candida albicans* in the Vagina: An Experiment with Vaginal Fluid

M.P. Bisschop, J.M. Merkus and J. Van Cutsem. Eur J Obstet Gynecol Reprod Biol 1985 Aug;20(2):113-9.

The growth of *Candida albicans* in fluid aspirated from the vagina of 18 women was studied. The growth of *C. albicans* in the aspirated vaginal fluid to which antibiotics were added proved to be enhanced in 16 out of 18 samples. The growth of *C. albicans* in Sabouraud medium proved not to be enhanced by the addition of antibiotics. Dilution of the Sabouraud broth and the reduction of the amount of added antibiotics did not change the outcome. It is concluded that enhancement of the growth of *C. albicans* in the vagina is not due to a direct growth-promoting effect of the antibiotics on the yeast. It is concluded that most probably the growth-promoting effect of antibiotics is obtained by way of an eradication of the bacterial flora harbored in the vagina.

Candidosis of the Genital Tract in Nonpregnant Women

P.M. Gough, D.W. Warnock, A. Turner, M.D. Richardson and E.M. Johnson. Eur J Obstet Gynecol Reprod Biol 1985 Apr;19(4):237-46.

Of 300 nonpregnant women seen in an STD clinic, 94 (31.3%) harbored *C. albicans* or *C. glabrata* in the genital tract; 84 of these women (89.4%) had at least one moderate or marked symptom or clinical sign. Of the 94 women with candida, 50 had another genital infection; 38 percent of these 50 women had at least one moderate or marked symptom or clinical sign, compared with 75 percent of the 44 women with no other infection. This difference is significant. Of the 146 women taking oral contraceptives, 51 (34.9%) had candida, compared with 43 (27.9%) of the 154 women who were not. The incidence of trichomoniasis, anaerobic vaginitis and nonspecific genital infection was lower among women with candida than among the others.

Is More than One Application of an Antifungal Necessary in the Treatment of Acute Vaginal Candidiasis?

L. Cohen. Am J Obstet Gynecol 1985 Aug 1;152(7 Pt 2):961-4.

The results of all the controlled trials carried out at the Department of Genito-Urinary Medicine at the Cardiff Royal Infirmary over the past 16 years are summarized. All except one of these trials were carried out with patients having acute vulvovaginal candidiasis. One trial involved treating only patients with recurring candidal infection. In all the acute trials, there were practically no mycologic relapses 7 days after completion of treatment whatever the regimen used, but at 35 days after completion of treatment the mycologic relapse rate was in the region of 20 percent to 25 percent. It is concluded that following the elimination of any known predisposing cause of vaginal candidiasis, the intravaginal application of 500 mg of an imidazole preparation is as effective a treatment as any other regimen. In recurrent cases, monthly treatment with such a dose may be adequate to control the patient's symptoms. Mycologic relapse may not be accompanied by symptoms, but in recurrent cases there is a closer relation between mycologic relapse and symptoms.

Recurrent and Persistent Vulvovaginal Candidiasis: Treatment with Ketoconazole

D.A. Eschenbach, D. Hummel and M.G. Gravett. Obstet Gynecol 1985 Aug;66(2):248-54.

Forty-two women were administered ketoconazole, an orally absorbed antifungal agent. The symptoms of vulvar pruritus, burning, pain, dysuria and the signs of vulvar erythema, fissures, and vaginal erythema were associated with *Candida albicans*. Although ketoconazole relieved symptoms and signs seven days after therapy, a high recurrence rate occurred by 28 days after therapy.

Influence of Estrogen and Normal Flora on Vaginal Candidiasis in the Rat

B. Larsen and R.P. Galask. J Reprod Med 1984 Dec;29(12):863-8

The vaginal epithelium of randomly bred albino rats normally does not contain yeast. This study demonstrated that estrogen-primed, castrated rats could be colonized by *Candida albicans* following intravaginal challenge, whereas rats not treated with estrogen remained resistant to colonization. The bacteriologic conditions of the vagina were also studied in yeast-colonized and non-yeast-colonized rats. No evidence of bacterial interference with yeast colonization was obtained from this study since the vaginal flora of the estrogen-treated, yeast-colonized rats was more abundant and diverse than that of the non-estrogen-treated rats, which were resistant to yeast colonization. Scanning electron microscopy of the vaginal epithelium of yeast-colonized rats showed that *C. albicans* entered the mycelial phase during colonization of the vagina. It also appeared that the mycelia penetrate the cornified vaginal epithelial cells.

Chancroid

The Comparative In Vitro Activity of Twelve 4-Quinolone Antimicrobials against *Hemophilus ducreyi*

R.A. Wall, D.C. Mabey, C.S. Bello and D. Felmingham. J Antimicrob Chemother 1985 Aug;16(2):165-8.

We have compared the in vitro activity of 12 quinolone antibiotics against 50 recent isolates of *Hemophilus ducreyi* from The Gambia. While these isolates were relatively resistant to the parent compounds, the newly synthesized quinolones exerted significant activity against *H. ducreyi*. Ciprofloxacin and ofloxacin were the most active compounds (MIC90 0.03 mg/l).

Comparative Study of Ceftriaxone and Trimethoprim-Sulfamethoxazole for the Treatment of Chancroid in Thailand

D.N. Taylor, C. Pitarangsi, P. Echeverria, K. Panikabutra and C. Suvongse. J Infect Dis 1985 Nov;152(5):1002-6.

A single dose of ceftriaxone (250 mg) administered intramuscularly was compared with trimethoprim-sulfamethoxazole (TMP-SMZ; 160/800 mg) administered orally twice daily for seven days or with a single dose of TMP-SMZ (640/3,200 mg) administered orally for the treatment of chancroid in men in Thailand. *Hemophilus ducreyi* was isolated from 79 (48%) of 164 men with a clinical diagnosis of chancroid. For men with ulcers that were culture positive for *H. ducreyi*, rates of cure were 100 percent in 25 men treated with ceftriaxone, 87 percent in 23 men given TMP-SMZ for seven days, and 55 percent in 31 men given TMP-SMZ in a single dose. For men with ulcers that were culture negative for *H. ducreyi*, rates of cure were 100 percent in 29 men treated with ceftriaxone, 66 percent in 32 men given TMP-SMZ for seven days, and 63 percent in 24 men given TMP-SMZ in a single dose. The MIC50 of the three antibiotics for 94 isolates of *H. ducreyi* were as follows: 0.004 micrograms/ml for ceftriaxone, 16 micrograms/ml for trimethoprim, and greater than 512 micrograms/ml for sulfamethoxazole. Our study indicates that ceftriaxone in a single dose of 250 mg is effective, but that TMP-SMZ, even when given in a standard seven-day regimen, is not effective treatment for chancroid in Thailand.

Trimethoprim Sulphamoxole in the Treatment of Chancroid. Comparison of Two Single Dose Treatment Regimens with a Five Day Regimen

J. Dylewski, H. Nsanze, L. D'Costa, L. Slaney and A. Ronald. J Antimicrob Chemother 1985 Jul;16(1):103-9.

In a prospective blinded study, 135 men with genital ulcers culture positive for *Hemophilus ducreyi*, were randomized to one of three regimens. Two single dose regimens, either the combination of sulphamoxole 3200 mg/trimethoprim 640 mg or trimethoprim 700 mg alone were compared to a five day regimen of sulphamoxole 800 mg/trimethoprim 160 mg twice daily. All 31 treated with a five day regimen of trimethoprim sulphamoxole healed without further treatment. Of 27 patients treated with the single dose sulphamoxole/trimethoprim regimen, only 21 were cured and of 34 treated with trimethoprim alone, 25 responded. Antibacterial susceptibilities were performed on 31 *H. ducreyi* isolates. The laboratory susceptibility of these strains to trimethoprim correlated with the clinical response to the single agent. Trimethoprim alone in a dose of 700 mg or the combination of sulphamoxole (3200 mg) and trimethoprim (640 mg) is not satisfactory for the single dose treatment of genital ulcer disease. However, when prescribed for five days, sulphamoxole/trimethoprim is effective and compares favorably with other treatment regimens.

An Outbreak of Chancroid in Orange County, California: Descriptive Epidemiology and Disease-Control Measures

C.A. Blackmore, K. Limpakarnjanarat, J.G. Rigau-Perez, W.L. Albritton and J.R. Greenwood. J Infect Dis 1985 May;151(5):840-4.

From May 1981 through February 1983, greater than 1,700 patients were examined for genital ulcers at the Orange County Special Diseases Clinic in Santa Ana, California. Of these patients, 923 had either confirmed chancroid or genital ulcers of unknown etiology. *Hemophilus ducreyi* was recovered from lesions or inguinal buboes of 271 patients. In the previous year, no cases of chancroid were reported in this community. Men accounted for 266 (98%) of the confirmed cases; 95 percent of the men were Hispanic, and at least 53 percent had had sexual contact with a prostitute. All five culture-positive women were prostitutes. Antimicrobial sensitivity testing showed resistance to both sulfamethoxazole and tetracycline but susceptibility to erythromycin and to the combination trimethoprim-sulfamethoxazole. Treatment of patients with chancroid, their sex partners, and temporarily incarcerated prostitutes contributed to the successful control of this outbreak.

Chancroid or Chancroidal Ulcers

V.N. Sehgal and A.L. Shyam Prasad. Dermatologica 1985;170(3):136-41.

One thousand five hundred thirty-two cases with genital ulcers were investigated, of whom 610 presented with features suggestive of chancroid; classic, multiple lesions of chancroid were observed in 312, while its other variants, i.e. dwarf, giant, and phagedaenic chancroid were also seen. In addition, 162 cases had a conspicuous morphology characterized by a single ulcer which was well-defined, soft, tender, non-indurated, and had weakening edges. These were termed chancroidal ulcers. The latter had a longer incubation period of 8-11 days. Absence of lymphadenopathy was prominent in these cases. The male/female ratio was 27/1. Persons of low socio-economic status in the sexually vulnerable age-group were predominantly affected. The prepuce, coronal sulcus and glans penis were the common sites of affliction in males, while the labia minora was frequently involved in females. Due to the limited value of gram-stained smears for the detection of *H. ducreyi* and lack of good culture media, chancroid and chancroidal ulcers should be differentiated clinically.

Thiamphenicol in the Treatment of Chancroid in Men

A.S. Latif, P.R. Crocchiolo and R. Lencioni. Sex Transm Dis 1984 Oct-Dec;11(4 Suppl):454-5

Fifty-five men were treated for culture-positive chancroid with two 2.5-g doses of thiamphenicol given on each of two consecutive days. Forty-nine patients (89.1%) were cured on this regimen. No adverse effects were noted. Cultured strains of *Hemophilus ducreyi* were found to be sensitive to thiamphenicol.

Cefotaxime Treatment of *Hemophilus ducreyi* Infection in Kenya

F.A. Plummer, N. Maggwa, L.J. D'Costa, H. Nsanze, P. Karasira, I.W. Maclean and A.R. Ronald. Sex Transm Dis 1984 Oct-Dec;11(4):304-7

The authors conducted a double-blind randomized clinical trial comparing single-dose cefotaxime (1 g im) plus daily placebo injections with cefotaxime (1 g im on each of three days). Each regimen was given with probenicid (1 g orally) for the treatment of chancroid. Twenty *Hemophilus ducreyi* culture-positive men received the single-dose cefotaxime regimen; in eight patients ulcers or buboes failed to respond to therapy. Nineteen *H. ducreyi* culture-positive men received cefotaxime on each of three days; *H. ducreyi* was eradicated from all patients, but one had a continuing ulcer and another had a bubo that failed to respond. Thus cefotaxime (1 g im daily for three days) plus probenicid (1 g orally) is effective therapy for chancroid. The lack of efficacy for chancroid of the single-dose cefotaxime regimen is surprising, given the remarkable susceptibility of *H. ducreyi* to cefotaxime; presumably the half-life of cefotaxime is too short for predictable eradication of *H. ducreyi* from the ulcer with a single-dose regimen.

Genital Molluscum Contagiosum

Laser Therapy for Vulvar Molluscum Contagiosum Infection

M.S. Amstey and G.C. Trombetta. Am J Obstet Gynecol 1985 Dec 1;153(7):800-1.

Multiple molluscum epidermal infections of the vulva are difficult to treat. Use of the carbon dioxide laser makes treatment easier, faster, and less uncomfortable than the historical method of curetting the lesions.

Group B Streptococcal Infection

Perinatal Complications in Group B Streptococcal Carriers: A Longitudinal Study of Prenatal Patients

J.R. Bobitt, J.D. Damato and J. Sakakini, Jr. Am J Obstet Gynecol 1985 Mar 15;151(6):711-7.

Although prenatal group B streptococcal detection and eradication have been proposed to prevent morbidity, the risk of perinatal complications in prenatal carriers of group B streptococci has not been defined. We evaluated 718 prenatal patients with serial cultures to compare morbidity in carriers and noncarriers. Complications occurring more frequently (p less than or equal to 0.05) in prenatal carriers were: collective morbidity, low birth weight, and premature rupture of membranes associated with low birth weight. Maternal pelvic infection and neonatal sepsis were increased in colonized women at delivery but not in prenatal carriers. Ninety-two percent of colonized women were not delivered of low birth weight infants. No carriers delivered vaginally or by repeat cesarean section became infected. Neither inoculum size nor chronic carriage was related to morbidity. The predictive value of a positive prenatal culture did not exceed 8 percent for any of the complications. We concluded that overall morbidity in carriers of group B streptococci is greater than in noncarriers; however, the risk for specific complications is too low to justify routine testing for detection of group B streptococci until prospective study demonstrates the value of such programs.

Is Group B Streptococcal Screening During Pregnancy Justified?

C.S. Easmon, M.J. Hastings, J. Neill, B. Bloxham and R.P. Rivers. Br J Obstet Gynaecol 1985 Mar;92(3): 197-201.

Twenty-eight percent of women investigated during pregnancy were carriers of group B streptococci (GBS). The use of broth enrichment was the most significant factor in determining GBS carriage rates. GBS carriage decreased during pregnancy. Transmission of GBS from mother to baby was related to vaginal carriage but rectal carriage in pregnancy was the best predictor of maternal carriage at term. Rectal and vaginal swabs taken at 28 and 36 weeks correctly predicted 92 percent of intrapartum GBS carriage. Although accurate prediction of intrapartum GBS carriage is possible, mass screening for GBS in pregnancy is unlikely to be cost-effective in those countries with a low incidence of neonatal GBS sepsis.

Early Neonatal Group B Streptococcal Disease: Degree of Colonization as an Important Determinant

L.J. Gerards, B.P. Cats and J.A. Hoogkamp-Korstanje. J Infect 1985 Sep;11(2):119-24.

During a period of 5 years (January 1, 1977 to January 1, 1982), 145 infants colonized with group B streptococci (GBS) were admitted to the neonatal intensive care unit of the University Children's Hospital, Utrecht. In 87 of these infants (60%), vertical transmission of GBS was established; in 43 of these 87 infants (49%), the degree of colonization was moderate to heavy. Early-onset (EO) GBS disease arose in 21 of 145 infants (attack rate: 14.5%). Of the 43 infants moderately to heavily colonized with GBS, however, 19 suffered from EO GBS disease (attack rate: 44.2%), whereas there were only two cases among the 44, lightly colonized infants (attack rate: 4.5%), a highly significant difference (P less than 0.0005). Similarly, probable sepsis (PS), defined as signs and symptoms of sepsis but without positive blood cultures, was observed significantly more often in moderately to heavily colonized infants (15/43, attack rate: 34.9%) compared with those lightly colonized (4/44, attack rate: 9.1%) (P less than 0.005). Infants moderately to heavily colonized with GBS at birth appear to have a significantly higher risk of developing serious GBS disease (EO or PS) than do infants only lightly colonized.

Cervicitis and Urethritis Caused by Group B Streptococcus: Case Report

G. Buttigieg. Genitourin Med 1985 Oct;61(5):343-4.

Group B streptococcus is not often isolated by gynecologists when a clinical diagnosis of cervicitis is made. I report on a patient suffering from cervicitis and urethritis caused by this organism, whose symptoms completely resolved after she was treated with phenoxymethylpenicillin.

Lymphogranuloma Venereum

Histological, Immunofluorescent, and Ultrastructural Features of Lymphogranuloma Venereum: A Case Report

B. Alacoque, H. Cloppet, C. Dumontel and G. Moulin. Br J Vener Dis 1984 Dec;60(6):390-5

We studied the course of a case of lymphogranuloma venereum (LGV) over two years. The comparative histological, immunological, and ultrastructural studies showed the existence of characteristic granulations within the macrophages of the granuloma. We suggest that direct immunofluorescence is a specific method for diagnosing cutaneous LGV. Some ultrastructural aspects lead us to believe that different chlamydial bodies exist inside the granuloma.

Reiter's Syndrome

Infectious Involvements in Males with Reiter's Syndrome

A.H. Vilppula, K.M. Granfors and U.I. Yli-Kerttula. Clin Rheumatol 1984 Dec;3(4):443-9.

To obtain data on infectious involvements contributing to joint attacks in Reiter's syndrome (RS), 72 consecutive males with RS were investigated. Controls were 219 personally interviewed males. A history of some type of oronaso-pharyngeal or pulmonary infectious involvements were reported as often in the patients as in the controls, but the frequency of persons with a history of joint manifestations followed by these infections was significantly higher in the patients (23/72) than in the controls (8/219) (p less than 0.0001). Gastrointestinal involvements occurred only in a minority of cases as a triggering infection. Histories of prostatitis, gonorrhea, *Condylomata acuminata*, hematuria and *Trichomonas vaginalis* infections were significantly more common in patients than in controls (p less than 0.001 – p less than 0.025). This finding, as well as evidence of chlamydial infection in 61 percent, speaks in favor of the importance of sexually transmitted diseases as an etiologic agent. A case report of triggering infections during the course of RS is given and the possible role of these infections in the immunopathogenesis in RS is discussed.

Viral Hepatitis

Immune Response after Vaccination with Recombinant Hepatitis B Vaccine as Compared to that after Plasma-Derived Vaccine

R.A. Heijtink, J. Kruining, M. Bakker and S.W. Schalm. Antiviral Res 1985;Suppl 1:273-9.

Thirty-one individuals (health care workers) were vaccinated with recombinant hepatitis B vaccine (10 microgram dose) and their immune response (anti-HBs) was compared to that of twenty-five health care workers after vaccination with plasma-derived vaccine (20 microgram dose). Although the seroconversion rate and the percentage of anti-HBs/a antibodies at month 7 were comparable, the geometric mean titre of anti-HBs at month 7 was considerably lower for the recombinant vaccine group (857.4 vs. 6736.5 IU/l). However, vaccinees from the two groups showing seroconversion at month 1 had comparable titres at month 7. Raising the dose of HBsAg in the recombinant vaccine may favorably influence the seroconversion rate at month 1 and thereby the immune response after three injections.

Altered Natural History of Hepatitis B in Homosexual Males—A Reflection of Altered Immune Responsiveness?

M.G. Anderson, A.L. Eddleston and I.M. Murray-Lyon. J Med Virol 1985 Oct;17(2):167-73.

We suggest that subtle alterations in T-cell functions in male homosexuals makes them more likely to have silent anicteric hepatitis B infection, and perhaps more likely to become chronic carriers with significant chronic liver disease. This immunodeficiency might also explain why they respond less favorably to antiviral therapy. In future trials of antiviral therapy, homosexual males should be randomized separately. Further studies of the immunomodulatory effects of new and existing agents will be of value in designing drug regimes particularly suited to the treatment of homosexual HBV carriers.

Prevention of Perinatal Transmission of Hepatitis B Virus (HBV) to Children of e Antigen-Positive HBV Carrier Mothers by Hepatitis B Immune Globulin and HBV Vaccine

K. Kanai, A. Takehiro, H. Noto, M. Nishida, K. Takahashi, Y. Kawashima, Y. Igarashi, K. Matsushita and M. Shimizu. J Infect Dis 1985 Feb;151(2):287-90

The efficacy of hepatitis B immune globulin (HBIG) with two hepatitis B virus (HBV) vaccines was investigated for prevention of vertical transmission of HBV to infants born to e antigen-positive HBV carrier mothers. Infants received 150 mg of the F(ab')2 fraction of HBIG intravenously within 2 hours of delivery, and serum titers of antibody to hepatitis B surface antigen (anti-HBs) were kept greater than 1:4 (passive hemagglutination) by subcutaneous injection of HBIG thereafter. HBV vaccine was started three or six months after delivery. Of 50 infants older than nine months, 49 were actively immunized against hepatitis B surface antigen. Vaccine containing alum adjuvant immunized the infants in a shorter period than did vaccine without adjuvant. Serum titers of anti-HBs of actively immunized infants were well maintained afterward. None of the infants treated with HBIG and HBV vaccine was positive for serum antibody to hepatitis B core antigen at 12 months of age. No side effects were observed.

Prevention of Perinatal Transmission of Hepatitis B Virus: A Comparison Between the Efficacy of Passive and Passive-Active Immunization in Korea

W.K. Chung, J.Y. Yoo, H.S. Sun, H.Y. Lee, I.J. Lee, S.M. Kim and A.M. Prince. J Infect Dis 1985 Feb;151(2):280-6

In a study to compare the prophylactic efficacy of passive and passive-active immunization against hepatitis B virus (HBV) among newborn infants of HBV carrier mothers positive for hepatitis B e in Korea, both regimens resulted in effective protection against development of hepatitis B surface antigen (HBsAg): 10 of 12 recipients of hepatitis B immune globulin (HBIG) and 25 of 29 recipients of HBIG and vaccine during nine months of follow-up. Among untreated controls in the same population just before the present study, 12 of 16 developed HBsAg within nine months of birth. Seven recipients of HBIG and vaccine and four untreated infants who had HBsAg in their blood at birth were excluded. The declining antibody levels in infants who received only HBIG as compared with the rising antibody levels in infants who received HBIG followed by three doses of HBV vaccine suggest that long-term protection will be seen only in the latter group.

Immunogenicity of HBV Vaccine in Healthy Chinese Children

L.Y. Hwang, R.P. Beasley, C.E. Stevens and W. Szmuness. Vaccine 1983 Dec;1(1):10-2.

The immunogenic response of healthy Chinese children to three different doses of hepatitis B virus (HBV) vaccine was compared. One hundred susceptible children received two doses of 10, 20 or 40 micrograms a month apart. A month following the first dose, 33 percent of all the children had antibodies. The response rate rose to 78 percent a month later and 99 percent four months later. Ninety percent of the 100 children still had antibody at 12 months after vaccination was initiated. The response rate, antibody levels and persistence of antibody were directly related to the dose of vaccine and inversely to the age of children. No adverse reactions were observed.

Epidemiology and Clinical Impact of Hepatitis D Virus (Delta) Infection

I.M. Jacobson, J.L. Dienstag, B.G. Werner, D.B. Brettler, P.H. Levine and I.K. Mushahwar. Hepatology 1985 Mar-Apr;5(2):188-91.

We tested sera collected between 1976 and 1984 from 362 persons in a variety of epidemiologic categories with acute and chronic hepatitis B and from 76 hemophiliacs and drug addicts with hepatitis B antibodies for hepatitis D markers. Hepatitis D markers were common in hemophiliacs, drug addicts, Afghanistanis, prisoners, and hemodialysis patients; rare in persons from other hepatitis-B endemic areas, persons with sporadic hepatitis B and homosexual men; and absent in health-care workers and institutionalized mentally retarded persons. No change was observed in the frequency of this infection during the 9 years of this study. We found hepatitis D markers in 5 percent of patients with acute hepatitis B, 1 of 3 with fulminant hepatitis and in 4 (1 in a homosexual male) of 12 episodes of acute hepatitis in hepatitis B carriers. Hepatitis D markers were more frequent in chronic liver disease (18%) than in asymptomatic hepatitis B carriage (2%), but there was no association between severity of chronic hepatitis and hepatitis D. These findings indicate that, to date, health-care workers and institutionalized mentally retarded persons have been spared from infection with this agent but suggest that homosexual males may not continue to be spared. Even in an area nonendemic for hepatitis D, this agent contributed to 20 to 30 percent of chronic hepatitis B and acute hepatitis superimposed on chronic hepatitis B infection.

A Final Report on Safety and Immunogenicity of a Bivalent Aqueous Subunit HBV Vaccine

A.M. Prince, B. Brotman, R.H. Purcell and J.L. Gerin. J Med Virol 1985 Apr;15(4):399-419.

The bivalent form of an aqueous formalin-inactivated hepatitis B vaccine was evaluated for safety and immunogenicity in chimpanzees. To evaluate safety, five animals were inoculated intravenously with vaccine containing 500 micrograms HBsAg and two animals with 50 micrograms. None of these animals developed hepatitis or any serologic marker indicative of the presence of residual live virus in the vaccine. Twenty-four animals were used to evaluate immunogenicity and protective efficacy. Seven of these immunized animals produced weak or no anti-HBs responses. Two doses of 50 micrograms HBsAg given subcutaneously 1 month apart protected each of four animals that were challenged with 10(3.5) CID50 HBV at 6 and 12 months after immunization and protected three of four animals challenged at 24 months against development of hepatitis or HBsAg. Three of 4 animals in each group immunized with two doses of 20, 10, or 5 micrograms HBsAg were similarly protected when challenged 6 months after immunization. Thirteen of 20 immunized animals that did not develop HBsAg after challenge with HBV developed anamnestic anti-HBs or anti-HBc responses between 2 and 18 months after challenge, indicating minimal replication of challenge virus. The time of onset and frequency of occurrence of these delayed responses was related to the titer of anti-HBs at the time of challenge. False positive Ausab test results were observed in quarantined chimpanzees. These were neither preceded by appearance of HBsAg nor accompanied by development of anti-HBc. In most cases, these reactions were due to a reactant having a sedimentation coefficient and an electrophoretic mobility resembling that of IgM. This reactant generally did not appear to confer resistance to challenge with HBV. The humoral immune response was characterized as being entirely of the IgM class 2 weeks after immunization and switched entirely into the IgG class by 10-12 weeks after vaccine administration. At the time of challenge, all animals with antibody had anti-HBs of subtype a.

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Vaginitis

Clinical

Vaginal Discharge and *Gardnerella vaginalis*. Predisposing Factors

J.G. Hansen and H. Schmidt. Scand J Prim Health Care 1985 Sep;3(3):141-3.

A total of 284 women, in the reproductive years, with vaginal discharge from which only *Gardnerella vaginalis* (GV) had been isolated, entered a questionnaire study on the possible causal relation between presence of GV and type of menstrual hygiene, type of contraception, number of deliveries, infertility and number of sexual partners. A control group consisted of 225 women without vaginal discharge. The study showed that patients with GV significantly more frequently used tampons for menstrual hygiene, sought medical assistance for vaginal discharge more often, and had more sexual partners. On the other hand, no difference was found between the two groups as to type of contraception, number of previous deliveries, and unsuccessful attempts of getting pregnant.

Anaerobes and *Gardnerella vaginalis* in Nonspecific Vaginitis

L.V. Hill. Genitourin Med 1985 Apr;61(2):114-9.

Clinical evidence of bacterial vaginosis was present in 25 (35%) of 72 patients attending a London venereology clinic and correlated significantly with abnormal organic acids in vaginal secretions (24/25), with *Gardnerella vaginalis* on culture (17/25), with complaints of vaginal malodor (15/25), and with a relative scarcity of white blood cells in vaginal secretions. Anaerobic vaginal flora were presumptively identified by gas-liquid chromatographic analysis of organic acids found in vaginal secretions. The clinical criteria used to diagnose bacterial vaginosis included the presence of at least three of the four following characteristics: (a) a vaginal pH greater than or equal to 4.5, vaginal secretions that (b) were homogeneous, (c) contained "clue" cells, and (d) released a "fishy" amine odor when mixed with 10 percent potassium hydroxide. Because 17 of the 25 patients with clinical bacterial vaginosis had both chromatographic bacterial vaginosis and *G. vaginalis*, causative organisms were difficult to identify. None of the six patients who had *G. vaginalis* but not chromatographic bacterial vaginosis had clinical bacterial vaginosis, but seven of the 10 women with chromatographic bacterial vaginosis but not *G. vaginalis* had clinical bacterial vaginosis (p less than 0.02, chi 2 with Yates's correction). This finding supports the recent suggestions that anaerobes are important in the production of clinical signs of bacterial vaginosis.

Therapy

In Vitro and In Vivo Activity of Metronidazole against *Gardnerella vaginalis*, *Bacteroides spp.* and *Mobiluncus spp.* in Bacterial Vaginosis

B.M. Jones, I. Geary, A.B. Alawattegama, G.R. Kinghorn and B.I. Duerden. J Antimicrob Chemother 1985 Aug;16(2):189-97.

An open, randomized, culture-controlled clinical study was designed to compare the efficacy of a single 2 g dose of metronidazole (Elyzol) with standard 7-day therapy in the treatment of bacterial vaginosis (BV). Forty-one of 47 (87%) patients given the single dose and 30 of 33 (91%) given the 7-day treatment were found to be cured seven days after treatment. At final assessment, 24 of 34 (71%) patients given the single dose and 22 of 28 (79%) given the 7-day treatment remained cured. The two regimes were equally efficaceous in eradicating *Gardnerella vaginalis*, *Bacteroides spp.* and *Mobiluncus spp.* (anaerobic curved rods) from vaginal specimens from patients with BV. The in vitro activity of metronidazole and its hydroxy metabolite was determined for 11 strains of *G. vaginalis*, 17 strains of *Bacteroides spp.* and 14 strains of *Mobiluncus spp.* which had been isolated from patients prior to treatment. The MIC of metronidazole against *G. vaginalis* varied between 2 and greater than or equal to 128 mg/l (median MIC 32 mg/l), but the hydroxy metabolite showed a markedly increased activity against eight of the strains tested (median MIC 4 mg/l). The MIC of metronidazole against the *Mobiluncus spp.* varied between 0.5 and greater than or equal to 128 mg/l (median MIC 16 mg/l) and the hydroxy metabolite showed little increased activity (median MIC also 16 mg/l). The Bacteroides organisms were highly susceptible to metronidazole and to the hydroxy metabolite, each having a median MIC of 1 mg/l.

Bacterial Vaginosis. An Evaluation of Treatment

P. Piot. Scand J Urol Nephrol (Suppl) 1984;86:229-35.

Various treatment regimens for bacterial vaginosis are reviewed. Orally administered metronidazole and tinidazole have been consistently successful, whereas widely variable results have been published from use of peroral ampicillin or tetracycline and from locally applied sulphonamide cream. The rationale for different treatments is discussed, with particular regard to the pathogenesis of the disease.

Susceptibility of *Gardnerella vaginalis* to Thiamphenicol: Clinical Experience with Nonspecific Vaginitis

J.M. Hubrechts, R.L. Vanhoof, A. Daems and J.P. Butzler. Sex Transm Dis 1984 Oct-Dec;11(4 Suppl):456-9

We compared the in vitro activity of thiamphenicol against 100 strains of *Gardnerella vaginalis* with the activity of 11 other antimicrobial agents. The MICs for thiamphenicol ranged from 0.39 micrograms/ml to 6.25 micrograms/ml. The concentration at which 50 percent of strains were inhibited (MIC50) was 1.96 micrograms/ml, and the concentration at which 90 percent of strains were inhibited (MIC90) was 3.93 micrograms/ml. All strains were very susceptible to erythromycin, chloramphenicol, beta-lactam antibiotics, and clindamycin. Tetracycline and metronidazole were only moderately active. In an attempt to cure *G. vaginalis*-associated vaginitis with a single-dose treatment, we administered 2.25 g of thiamphenicol to 20 volunteers; 17 were clinically and bacteriologically cured. In two cases, we observed that *G. vaginalis* was not eliminated immediately (i.e., at the first follow-up visit), but we saw a progressive disappearance of the strain without further treatment. In one case the treatment seemed to have failed but reinfection could not be ruled out. The results show that a single dose of thiamphenicol can cure *G. vaginalis*-associated vaginitis.

Treatment of Vaginal Candidosis with Tioconazole 2% Vaginal Cream

M. Leegaard. Acta Obstet Gynecol Scand 1985;64(2):127-9.

Six hundred and three women in a contraceptive clinic were examined for the presence of *C. albicans* in the vagina and questioned about symptoms. Twenty-nine women with *C. albicans* accompanied by symptoms were treated with tioconazole 2 percent in a vaginal cream for 3 days, repeated once after an interval of 1 week. The mycological cure rate was 88.5 percent. At the same time, 34 women with vaginal *C. albicans* but without symptoms were examined. The spontaneous cure rate in these patients was 58.8 percent. In the symptomatic group, rectal *C. albicans* was observed in 56.5 percent of patients before treatment. After vaginal treatment, a rectal cure rate of 100 percent was achieved, but with a recurrency frequency after 2-4 weeks of 17.4 percent. Comparative vaginal recurrency frequency was 10.3 percent. Three were not cured. The method used has shown itself to be very acceptable for the patient and to have a cure frequency that is fully equal to previously used, longer lasting treatments.

Ketoconazole in the Treatment of Vaginal Candidiasis

B. Bloch and E. Smythe. S Afr Med J 1985 Feb 2;67(5):178-9.

In a preliminary open prospective study ketoconazole (Nizoral; Janssen) 200 mg twice daily for 5 consecutive days was found to be extremely effective in treating vulvovaginal candidiasis, producing cure rates of 96 percent at 7 days and 92 percent at 28 days. The oral route of administration has definite advantages over the vaginal route and improves patient compliance. No side-effects related to treatment were found in this study.

The Treatment of *Trichomonas vaginalis* Vaginitis. An Open Controlled Prospective Study Comparing a Single Dose of Metronidazole Tablets, Benzoyl Metronidazole Suspension and Tinidazole Tablets

B. Bloch and E. Smyth. S Afr Med J 1985 Mar 23;67(12):455-7.

Metronidazole tablets, benzoyl metronidazole suspension, and tinidazole tablets each given as a single 2 g bolus dose in an open controlled prospective study were found to be effective forms of treatment for *Trichomonas vaginalis* vaginitis. The cure rates on wet smear preparations were 100 percent, 100 percent and 94.8 percent, respectively, and symptomatic and observed improvements were excellent. There was a statistically significant difference between the response rates associated with both metronidazole preparations and tinidazole. The results of this study indicate that single-dosage bolus therapy can confidently be recommended in trichomonal infections and that it has a number of advantages.

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Sexually Transmitted Diseases — Pregnancy

Sex Education Needs and Interests of High School Students in a Rural New York County

N. McCormick, J. Folcik and A. Izzo. Adolescence 1985 Fall;20(79):581-92.

Seventy-five boys and 88 girls from three high schools in a rural county of New York state took a sex education quiz and were asked to describe their sexual and contraceptive experiences and sex education interests. Consistent with most previous research, nonvirgin teenagers who earned better grades on the sex education quiz failed to use more effective contraceptives than nonvirgins who had performed poorly on the quiz. There was a striking similarity among students' descriptions of sex education interests, regardless of their gender, previous enrollment in a health course, or experience with sexual intercourse. Very few teenagers (9%) were completely satisfied with their high school's current sex education program. The majority (57%) wanted to learn more about contraceptives and venereal disease prevention, either as the primary focus of their sex education curriculum or in combination with other topics such as sexual values, the biology of reproduction, and information about the human body. Many adolescents (19%) seemed confused about their sex-education needs and described a vague interest in everything sexual. Only 2 percent of the students thought sex education should provide them with erotic information or techniques for increasing sexual pleasure. The remaining students wished that their sex education courses would give them additional information solely about sexual values (5%) or the biology of reproduction and knowledge about the body (8%).

Vaginal Douching as a Potential Risk Factor for Tubal Ectopic Pregnancy

W.H. Chow, J.R. Daling, N.S. Weiss, D.E. Moore and R. Soderstrom. Am J Obstet Gynecol 1985 Dec 1;153(7):727-9.

The incidence of ectopic pregnancy in the United States has more than doubled in the past decade. Because a previous study has suggested that the practice of vaginal douching may increase the risk of pelvic inflammatory disease, a condition known to predispose to ectopic pregnancy, and because the sale of commercial douching products in the United States has more than tripled since 1974, we investigated this practice as a possible risk factor. We interviewed 155 women who had a tubal ectopic pregnancy treated at five Seattle hospitals between 1975 and 1979 as to their reproductive, contraceptive, and medical histories, demographic characteristics, and personal hygiene practices. During the same period, 456 women who were delivered of a baby in King County were identified from Vital Records and interviewed as controls. A higher proportion of cases than controls reported ever having douched in the past. Cases also douched more frequently than controls. After simultaneous adjusting for confounding factors in our data by means of a multiple logistic regression technique, the risk of tubal ectopic pregnancy for women who douched at least weekly was twice that of women who never douched (95% confidence interval = 1.03 to 4.00).

Bacterial Vaginosis During Pregnancy. An Association with Prematurity and Postpartum Complications

D.A. Eschenbach, M.G. Gravett, K.C. Chen, U.B. Hoyme and K.K. Holmes. Scand J Urol Nephrol (Suppl) 1984;86:213-22.

Although bacterial vaginosis (BV) is a common disorder associated with high concentrations of potentially pathogenic micro-organisms, BV has not yet been linked to infections outside the vagina. To investigate the association of BV with adverse outcomes during or following pregnancy, we analyzed the prevalence of BV among women with and without premature labor, and early-onset postpartum endometritis. Bacterial vaginosis was identified by gas-liquid chromatographic criteria in 28 (49%) of 57 women giving birth at less than or equal to 37 weeks gestation or with birthweight less than 2500 g and in 27 (24%) of 114 women bearing an infant at term ($p = 0.001$). Organisms associated with BV, such as *Gardnerella vaginalis*, anaerobic bacteria, and/or genital mycoplasmas, were recovered from the endometrium of 61 of 101 women with clinical signs of endometritis. *G. vaginalis* was the most frequent isolate from both the endometrium (38 patients) and the blood (8 patients) of women with postpartum endometritis. *Bacteroides bivius* was the most frequent anaerobic isolate from the endometrium (11 cases) and blood (4 cases). Patients with both *G. vaginalis* and anaerobes isolated remained febrile significantly longer after beginning antibiotic therapy than did other patients (57.1 hours. vs. 36.3 hours, $p = 0.02$). These data suggest that BV may be associated with prematurity and that BV may contribute to postpartum maternal infectious morbidity.

Penicillin Allergy and Desensitization in Serious Infections During Pregnancy

G.D. Wendel, Jr., B.J. Stark, R.B. Jamison, R.D. Molina and T.J. Sullivan. N Engl J Med 1985 May 9;312(19):1229-32.

Penicillin allergy presents a major obstacle to the successful management of some antepartum infections. We studied 15 pregnant women with histories of penicillin allergy confirmed by positive immediate wheal-and-flare skin tests. Thirteen had syphilis, one listeria sepsis, and one *Streptococcus viridans* endocarditis. Each patient was desensitized over four to six hours by oral administration of increasing doses of penicillin V. At the completion of the procedure, full-dose parenteral therapy with penicillin G or ampicillin was instituted. No extracutaneous reactions were detected. Five of the subjects (33%) experienced pruritus (three) or urticaria (two), but no interruption of desensitization or therapy was necessary. All clinically apparent maternal infections were cured. The pregnancy complicated by listeriosis aborted in the first trimester. The 11 neonates delivered to date are normal. These results indicate that oral desensitization is an acceptably safe approach to therapy in pregnant women who are allergic to penicillin and have infections that require beta-lactam drugs.

Spontaneous Abortion — An Infectious Etiology?

P.E. Munday, R. Porter, P.F. Falder, J.M. Carder, R. Holliman, B.V. Lewis and D. Taylor-Robinson. Br J Obstet Gynaecol 1984 Dec;91(12):1177-80

The role of *Chlamydia trachomatis*, genital mycoplasmas, *Campylobacter spp.* and other aerobic and anaerobic bacteria in the etiology of spontaneous abortion was investigated prospectively in 241 pregnant women at a community hospital. Sixteen women who had threatened abortions were a little younger, of lower social class and had had more previous spontaneous abortions than the 76 women who aborted or the 149 women whose pregnancies were not complicated in the early stages by hemorrhage. The demographic characteristics of the latter two groups of women were similar. *C. trachomatis* was isolated from the cervix of only one woman and she had no genital tract bleeding at any stage in her pregnancy. *Mycoplasma hominis* was isolated most often from the women who had threatened abortions but otherwise the prevalence of the other various microorganisms was similar in women who had spontaneous abortions, threatened abortions, and in those who had pregnancies uncomplicated by vaginal bleeding. It was clear, therefore, that *C. trachomatis* played no role in the etiology of spontaneous abortion in the population studied and there was no suggestion that any of the other microorganisms were involved either.

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Pharmacology

Psychosis and Seizures Following the Injection of Penicillin G Procaine. Hoigne's Syndrome

T.J. Silber and L. D'Angelo. Am J Dis Child 1985 Apr;139(4):335-7.

Psychosis and/or seizures following the administration of intramuscular penicillin G procaine have not been reported in the pediatric literature to our knowledge. This omission is regrettable in light of the frequency with which this treatment is indicated as therapy for gonococcal infections. We report clinical data from four patients afflicted by this reaction known as Hoigne's syndrome. The dramatic and unexpected manifestation of this condition calls for an immediate diagnosis to proceed with the appropriate treatment.

A Controlled Trial of the Use of Erythromycin for Men with Asthenospermia

H.W. Baker, W.G. Straffon, M.P. McGowan, H.G. Burger, D.M. de Kretser and B. Hudson. Int J Androl 1984 Oct;7(5):383-8.

A double-blind crossover controlled trial of erythromycin was conducted in 78 men with asthenospermia (mean pretreatment sperm concentration greater than or equal to 20 X 10(6)/ml and motility less than 60%). Sperm motility increased above the pretreatment mean after the first one month course of treatment for both erythromycin (7.9 +/- 2.6% P less than 0.01; mean +/- SEM) and the placebo group (7.5 +/- 2.2% P less than 0.01) and also after the second one month course of treatment, given one month after the first, for both erythromycin (11.8 +/- 2.7% P less than 0.001) and placebo (11.4 +/- 2.8% P less than 0.001). There was no significant difference between the changes in sperm motility with erythromycin and placebo. Twelve pregnancies occurred during the four month trial time—eight with erythromycin and four with placebo (chi 2 = 2.51 P = NS). It is concluded that in infertile men, sperm motility tends to increase spontaneously with time. Erythromycin treatment has no significant effect on semen quality and a larger trial will be required to determine if erythromycin increases fertility.

Activities of New Quinoline Derivatives against Genital Pathogens

J. Aznar, M.C. Caballero, M.C. Lozano, C. de Miguel, J.C. Palomares and E.J. Perea. Antimicrob Agents Chemother 1985 Jan;27(1):76-8.

The in vitro activities of four quinoline carboxylic acids against 48 strains of *Neisseria gonorrhoeae*, 10 of *Chlamydia trachomatis*, and 32 of *Ureaplasma urealyticum* were compared. Ciprofloxacin was the most active against *N. gonorrhoeae* and *C. trachomatis* but had poor bactericidal activity against *U. urealyticum*, whereas ofloxacin showed the most bactericidal activity against *U. urealyticum* but was less active than ciprofloxacin against the two former pathogens. Norfloxacin and enoxacin were less active against all the studied pathogens.

Cross Allergenicity between Penicillins and Cephalosporins

T.R. Beam, Jr. and J. Spooner. Chemioterapia 1984 Dec;3(6):390-3.

Twenty patients excluded from pre-marketing trials of cephalosporin antibiotics as chemoprophylaxis for open heart surgery were enrolled in an evaluation of skin-test reactivity. All gave a history of type I hypersensitivity to penicillins. None knew of adverse reactions to cephalosporins. Eighteen were negative to testing with saline, cefazolin, ceftriaxone, penicillin G, and benzylpenicilloyl. Two patients with positive skin tests safely received vancomycin chemoprophylaxis. We conclude that most patients who give a positive allergic history but have negative skin tests can safely receive cephalosporin chemoprophylaxis.

Study of the In Vitro Activity of Norfloxacin and Other Drugs on Amoxicillin-Resistant Uropathogenic Isolates

R. Piccolomini, N. Allocati and G. Catamo. Chemioterapia 1984 Jun;3(3):167-72.

The in vitro activity of a quinolinecarboxylic acid compound, norfloxacin, was compared with those of amikacin, carbenicillin, cefazolin, cefoxitin, gentamicin, nalidixic acid, and oxolinic acid against 243 Gram-positive and Gram-negative amoxicillin-resistant (MIC 800 greater than or equal to micrograms/ml) uropathogenic isolates. Norfloxacin showed remarkable activity against the majority of the bacteria tested. Ninety percent of strains of *Staphylococcus aureus*, *Streptococcus faecalis*, *Citrobacter freundii* and *Serratia spp.* were inhibited by 3.12 micrograms/ml or less. Among the Gram-negative urinary isolates, only a few Enterobacter, *Escherichia coli*, Klebsiella, Proteus and *Pseudomonas aeruginosa* strains required norfloxacin levels between 12.5 and 25 micrograms/ml. The MBC was within one dilution of the MIC for 100 percent of the Gram-positive strains and 95 percent of the Gram-negative isolates against norfloxacin and aminoglycosides. Norfloxacin had a markedly higher inhibitory index than all other antimicrobial agents for Gram-positive cocci and Gram-negative bacteria. From its in vitro activity, norfloxacin appears to be a potentially valuable agent for the treatment of serious urinary tract infections.

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